BRAIN INJURY IN SENIORS IN BRITISH COLUMBIA: ITS RELATIONSHIP TO DEPRESSION AND CHRONIC PAIN

by

Janice Montbriand

BA, University of Regina, 2002
MSc, University of Northern British Columbia, 2006

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Abstract

Traumatic brain injury (TBI) represents a significant public health issue, not only within British Columbia, but within all of Canada. As the Canadian population ages, it will be important to have information on the antecedents and consequences of brain injury in the elderly. However, as TBI is more common in younger age groups, much of the research has not reflected the experience of seniors (Rapoport & Feinstein, 2000). The elderly are at increased risk for brain injury as they age, and for morbidity and mortality post-TBI (Maurice-Williams, 1999). Outcomes of TBI, including depression and chronic pain (CP), were examined. Cases with CP showed shorter survival time post-TBI than those without CP, after controlling for cancer. Compared to a control group of seniors without TBI, seniors post-TBI were at higher risk of developing depression. Risk of developing new cases of depression was linked to gender and non-traumatic brain injury. No set of variables predicted who would develop CP post-TBI. Logistic discriminant function analyses indicated that psychological variables such as anxiety and insomnia were more strongly associated with CP pre-TBI than non-CP pre-TBI.

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I. Introduction

Traumatic brain injury (TBI) represents a significant public health issue in Canada as it is an important cause of mortality and long term morbidity, particularly in the very young and very old (CIHI, 2006). It is estimated that there are nearly 200,000 cases of TBI a year in Canada, associated with close to 2 million days in hospital (CIHI, 2006). TBIs of varying levels of severity are associated with lifelong consequences in many domains of functioning, including psychological, cognitive, behavioural, physical, social, and daily living activity sequela (Bruns & Hauser, 2003). A proper understanding of the antecedents and consequences of TBI is critical for both prevention and optimal management.

Canada, along with other industrialized nations, is experiencing a demographic shift as the population ages. In 2005, 12.6% of the Canadian population was aged >65, and this number is expected to increase to 20.7% by the year 2025 (Ruggeri, & Zou, 2006). Risk of a TBI in Canada increases with age, most dramatically in those over age 70 (Pickett, Simpson & Brison, 2004). In Ontario, the rate of hospitalization for blunt head trauma was 85.3 per 100,000 in 1994/95, and decreased to 62.7/100,000 in 1998 (Picket, Simpson & Brison, 2004). The rates rose sharply for both men and women after the age of 70 (Pickett, Simpson & Brison, 2004). The Ontario Trauma Registry reports that TBI is the third most commonly reported injury in those over 65 years of age (Rapoport & Feinstein, 2000).

While a decrease in TBI rate is occurring in some industrialized countries, TBI rates in seniors have been increasing dramatically, leading Kannus, Miemi, Parkkari, Palvanen and Sievanen (2007) to conclude that "These injuries represent an alarming epidemic and the predicted ageing of populations will soon exacerbate the burden on our health care system" (p.

83, Bruns & Hauser, 2003; Masson et al., 2001). Some have contended that the decrease is occurring more in mild TBI than major head injuries (Pickett, Simpson & Brison, 2004).

As the Canadian population ages, it will be important to have information on the antecedents and consequences of brain injury in the elderly. It has also been suggested that information about features associated with the incidence of important illnesses/events could be used to identify where to effectively direct suitable interventions, such as the development of prevention programs, and anticipating projected health care costs (Hickey, Speers & Prohaska, 1997; Ruggeri & Zou, 2006). However, as TBI has been more common in younger age groups, research has not always reflected the experience of seniors (Rapoport & Feinstein, 2000). TBI prevention programs not specific to the elderly will "often neglect the special issues of the older adult" (Thompson, McCormick & Kagan, 2006, p.1590). Other issues that need to be addressed include the fact that estimates of TBI often include only hospital cases, leading to an underestimation of TBI in both youth and seniors (Rapoport & Feinstein, 2000). Also, few studies have looked at how psychological comorbidities such as depression and chronic pain (CP) can affect the outcome of TBI in seniors. This study will look at CP as a risk factor for worse outcomes post-TBI in the elderly, as well as the risk of development of depression post-TBI in the elderly.

Psychological Sequela of TBI

It has been suggested that psychological sequela can be some of the most disabling deficits associated with TBI, and have a negative impact on rehabilitation and quality of life (QOL; Bombardier et al., 2010; Rapoport, McCullagh, Shammi & Feinstein, 2005; Rogers & Read, 2007). Skell et al. (2000) noted that behavioural and emotional factors contribute strongly to post-TBI disability levels/adjustment difficulties and, in the long term, are the most common

self-reported problems associated with TBI. In his review, Menzel (2008) commented upon the dearth of studies on pre-TBI psychological disorders, which he found 'startling and troubling', and emphasized the need for studies that included older age groups and stricter age requirements.

Definition of Traumatic Brain Injury (TBI)

The World Health Organization created a definition of acquired brain injury which is also currently being used by the province of British Columbia:

"Damage to the brain, which occurs after birth and is not related to a congenital or a degenerative disease. These impairments may be temporary or permanent and cause partial or functional disability or psychosocial maladjustment" (BC Brain Injury Association, http://www.bcbraininjuryassociation.com/acquired.php, accessed 2012).

This definition helps to differentiate acquired brain injuries from congenital ones, or brain injury related to disease such as Alzheimer's. TBI has been defined as:

"An alteration in brain function manifest as confusion, altered level of consciousness, seizure, coma, or focal sensory or motor neurologic deficit resulting from blunt or penetrating force to the head. In mild TBI, subtle behavioural and neuropsychological changes may be the only symptoms" (Bruns & Hauser, 2003, p.65).

The BC Brain Injury Association also states that, in British Columbia, 14,000 people sustain a new TBI each year. Motor vehicle accidents (MVAs) are the leading cause of acquired brain injuries (BC Brain Injury Association, http://www.bcbraininjuryassociation.com/acquired.php). However, this pattern shifts with age and, in the elderly, unintentional falls are the most common cause of traumatic brain injury (Selman & Benzel, 1999).

Type and Severity of TBI

Mild, Moderate and Severe TBI. When classifying TBI severity, the Glasgow Coma Scale (GCS) is the measure most commonly used. The GCS involves measuring patient eye movement responsiveness, verbal functioning and level of consciousness and categorizes the level of TBI as either mild, moderate, or severe (Bruns & Hauser, 2003). However, most TBI studies are based on large epidemiologic datasets. As these sets may not have been intended for research, it is more common for the type rather than the severity of the TBI to be recorded. This can make it quite difficult to estimate the severity of the TBI. Pickett, Simpson and Brison (2004) used a proxy measure by categorizing the TBI into groups by type (Concussion, hemorrhage, etc).

The under-reporting of mild traumatic brain injury (mTBI) is also a problem, and has led some to call it "the silent epidemic," where, in Ontario, "the majority of patients with mild TBI go undiagnosed" (Feinstein & Rapoport, 2000, p.325). Estimates indicate that only 20% of head injuries fall in the moderate-to-severe category, with 80% of head injuries being mild (Bruns & Hauser, 2003). This may be especially true in seniors for similar reasons as to why abuse is under-reported: it is possible that smaller social networks and medical conditions preventing them from reporting the injury.

Type of TBI.

Little research has been done using multiple database types when looking at psychological variables in relation to TBI. One of the issues is the measurement of TBI. Both hospital and the medical services payment plan files contain ICD-9 billing codes, including codes that are used to identify different types of TBI. Categories based on rough severity of TBI can then be formed.

Pickett, Simpson and Brison (2004) conducted a study of blunt head trauma in Ontario using the population-based Ontario Trauma Registry. ICD-codes extracted from the database included: N800-804 (skull fractures); N850 (concussion); N851 (cerebral laceration and contusion); N852-853 (hemorrhages); N854 (intracranial injury unspecified). The present analysis used very conservative criteria for TBI, in which ICD injury codes were grouped in order of increasing severity: 850 (concussion), 800-804 (skull fractures), 851, 854 (intracranial injury) and 853-852 (intracranial with hemorrhage).

TBI in Seniors

The cut-off age designated for seniors in TBI studies ranges from the 50s to the 70s (Rapoport & Feinstein, 2000). The present study was based on the definition of a senior as someone over the age of 65, as this is most common and accepted cut-off age (Rapoport & Feinstein, 2000; Selman & Benzel, 1999). Selman and Bezel (1999) support the use of this age cut-off in Western countries as it is the usual age of retirement.

Corrigan, Selassie and Orman (2010) note that the incidence of TBI in the United States for those greater than 74 years of age is estimated at 659 per 100,000. This increased risk grows with age, and those aged 85 years or older are at the highest risk for TBI (Bruns & Hauser, 2003). Masson et al. (2001) found that there was a peak risk of severe brain injuries in those over age 70, the same age at which mortality rates increase dramatically. Males continued to be at a higher risk of a severe TBI throughout life.

Overall statistics for TBI that do not take age into account will risk missing shifts in TBI rates that occur with age (Bruns & Hauser, 2003). Studies have noted a "trimodal age specific TBI incidence" where TBI rates peak once in initial childhood, once in later adolescence, and again in the older adulthood (Bruns & Hauser, 2003; Selman & Benzel, 1999). Once a person is

65 years of age or older, risk for TBI increases considerably, and research suggests that those greater than 70 years of age show the highest rate of TBI (Masson et al., 2001; Raporport & Feinstein, 2000). Newer research has described an 'alarming' rise in severe head injuries in older seniors. For example, Kannus, Niemi, Parkkari, Palvanen and Sievanen (2007) followed a group of older seniors (>80 years) for five years in Finland, and found that the age-adjusted incidence of severe TBI caused by falls in older seniors increased by over 200% in both men and women. The authors contend that this dramatic increase in TBI due to falls cannot be explained by an aging population alone, highlighting the increased risk attributable to falls and the importance of fall prevention for seniors.

Seniors fare less well after head injuries than younger persons, even in cases of mild TBI (Selman & Benzel, 1999). Seniors over 75 years of age show the highest fatality rate compared to any other age group (Corrigan, Selassie & Orman, 2010). Seniors who were already living in institutional settings fared worse after falls and head injuries than community-living seniors (Rubenstein, 2006).

Abelson-Mitchell (2008) suggested that the elderly are more vulnerable as "soft targets", meaning that they are relatively unprotected from, or especially vulnerable to, the effects of TBI (p.54). Seniors are more susceptible to injury due to both age-related changes and a higher level of co-morbidities. This may also prolong recovery, leading to greater risk of repeated falls (Rubenstein, 2006). "Elderly patients account for more than 50% of the deaths that result from trauma, even though they make up only 30% of admissions" (Gowing & Jain, 2007, 440). Why this occurs is a matter of debate. One theory holds that there is simply a smaller physiological reserve to fall back on in seniors compared to younger persons (Gowing & Jain, 2007; Selmen & Benzel, 1999). The brain is less plastic with age, so less able to reorganize itself after injury. The

risk of both physical and cognitive frailty increases with age, and this may make seniors more susceptible to the effects of TBI (LeBlanc et al., 2006).

Not all studies have been in agreement that seniors are at immediate increased risk of worse outcomes post-TBI. While studies of moderate to severe TBI have been consistent, studies of mild TBI have not. For example Rapoport and Feinstein (2001) found, when comparing 26 seniors to 30 controls one year post-TBI, that not all outcomes measured (such as psychosocial impairment) reached statistical significance. They hypothesized that seniors not having to return to work may find fewer social and psychological stresses post-TBI. Once work status was controlled for, seniors did show a tendency towards lower levels of global functioning ($p=.03$), psychosocial impairment ($p=.04$) and psychosocial distress ($p=.04$). The authors also postulated that as post-TBI effects include accelerated aging, age-related differences may become more obvious the longer the passage of time post-TBI.

TBI and Gender

Males make up the largest proportion of TBI victims in all age groups cross-culturally, and are more likely than women to have a more severe TBI (Ableson-Mitchell, 2008; Annagers et al., 1980; Maurice-Williams, 1999, Selman & Benzel, 1999). This difference is most pronounced in younger age groups (Burns & Hauser, 2003). The rate of TBI in men overall is twice that in women, and the rate of male fatalities due to TBI in the USA is 3.4 times higher than in women (Corrigan, Elassie & Orman, 2010). The male to female ratio in TBI is the highest for injuries induced by MVAs and assaults (Bruns & Hauser, 2003). Males are also more likely to have alcohol as a contributing factor in a TBI (Maurice-Williams, 1999). Interestingly, in the oldest group, there is an approximately equal rate of TBI across the sexes possibly due to a decrease in MVAs and assaults (Burns & Hauser, 2003; Wong, Dornan, Schentag, Ip & Keating ,

1993). One study found the female to male ratio of TBI in U.S. seniors over 80 was 3:2 (Amacher & Bybee, 1987).

Psychological Factors in TBI

While both male and female seniors may be at decreased risk of some psychological disorders with age, the presence of one or more psychological disorders is associated with worse outcomes post-TBI (Streiner, Cairney & Velhuizen, 2006). One area of contention is whether it is the co-morbidities themselves, or the polypharmacy associated with them, that leads to increased risk of falls and TBI in seniors. Authors of a meta-analysis came to the conclusion that it was the comorbidity rather than the medications that explained the increased risk (Leipzig, Cummings, & Tinetti, 1999).

Depression.

Pre-TBI depression.

Depression is a modifiable risk factor for falls and TBI. For example Stalenhoef, Diederiks, Knottnerus, Kester and Crebolder (2002) found that depressive mood was a predictor of recurrent falls in a community-dwelling population (O.R.= 2.2). Therefore early identification and intervention of depression in seniors may be important, both in rehabilitation, and also in prevention of TBI (Bombardier et al., 2010; Rapoport et al., 2005; Streiner et al., 2006; Vassallo, Proctor-Weber, Lebowitz, Curtiss & Vanderploeg, 2007). It would be important to evaluate whether or not treating depression had the intended effect of lowering rates of falls in this population.

Bombardier et al. (2010) found that depression pre-TBI was associated with an increased risk of post-TBI depression, as well as the development of post-TBI anxiety disorders. Some studies have suggested that younger age groups may be at higher risk of post-TBI depression

than older age groups, although not all of these studies include an older senior population (Hart et al., 2011). Studies also suggest that women are at higher risk of post-TBI depression than men, but the results have not been entirely consistent (Hart et al., 2011). Given that seniors are at higher risk of negative outcomes post-TBI than non-seniors, the effect of pre-TBI depression and/or gender may be more prominent in this population.

Depression has also been linked to another important risk factor for falls and TBI, chronic pain. Szerbinska, Hirdes and Zyczkowska (2012) found that depression is currently undertreated in seniors in Canada, and is related to self-reported daily pain. They were unable to determine which of these factors was the initiator of this relationship, and suggested that the relationship was likely reciprocal, with under-treatment of pain possibly playing a role in depression.

A shortcoming of current research is that investigations into pre-TBI psychological disorders have relied almost solely on retrospective self-report. Gould, Ponsford, Johnston and Schonberger (2011) attempted to fill in some gaps by following individuals prospectively, and found that pre-injury psychological disorders were independently predictive of poorer psychosocial outcome post-TBI. The authors noted that no studies to date had the ability to look at the relationship between pre-TBI anxiety and outcome. In the present study, the use of pre-injury medical and pharmaceutical data to identify psychological disorders will enable some of these gaps to be addressed.

Post-TBI depression. Depression is the prevailing psychological issue post-TBI in the general population, with up to 30% experiencing post-TBI depression within the first year (Pagulayan, Hoffman, Timken, Machamer & Dikmen., 2008; Rapoport, 2012). One study estimates the incidence of new cases of depression post-TBI to be 49% (Hart et al., 2011).

Depression, both pre- and post-TBI, is a risk factor for poorer outcome and less effective/more costly rehabilitation (Bombardier et al., 2010; Stonnington et al. 2001). However, many studies investigating the relationship between depression and TBI have excluded older populations (Rapoport, McCullagh, Streiner & Feinstein., 2003a).

Depression itself may be a risk factor for falls, head injury, and poorer recovery post-injury. Van den berg et al. (2011) found that in women aged 60 years and over, the development of depression following a variety of low-energy fractures (hip, finger, toe, etc.) led to an increased risk of further falls. Post-TBI depression has been linked to lower scores in verbal memory, processing speeds, working memory, and executive function, all of which are increasingly important in an elderly population (Hart, 2011). Recent studies suggest decreased processing speed has been linked to an increased risk of falls in older adults (Sosnoff et al., in press). In the very old, falls are the leading cause of TBI. Van den berg et al. (2011) concluded by suggesting that doctors check for, and treat, depression post-TBI to prevent an increase in falls.

Post-TBI depression is associated with a lower WOL, increased problems with mobility, increased levels of pain, and lower living skills as well as poorer interpersonal relationships (Bombardier et al., 2010; Hart et al., 2011; Whelan-Goodinson, Ponsford & Schonberg, 2008). Both depression and anxiety were related to lower levels of independence. Rapoport, Kiss and Feinstein (2006) followed a group of 77 older adults with mild to moderate TBI over a period of one year. As measured at two months post-TBI, approximately 16% of cases met the criteria for depression. Depression at 2 months was associated with poorer outcomes at one year, such as higher levels of post-concussive symptoms and increased problems with activities of daily living when compared to those without depression.

Pagulayan et al. (2008) investigated the directionality of this relationship in a middle-aged sample. The authors found that depression levels tended to increase following higher levels of perceived injury-related changes rather than preceding these changes in cases of mild to moderate TBI. However studies have suggested that treating post-TBI depression can aid rehabilitation efforts. For example, in a Canadian study, Rapoport, McCullagh and Shami (2003b) broke down the negative effects of combined depression and TBI on QOL into: 1) mood, 2) cognitive dysfunction, and 3) increased economic burden post-TBI, due to lower recovery. They found that TBI and depression shared common cognitive complaints, such as slower processing speed, and deficits in working memory (WM) and executive function. The authors suggested that depression was a marker of poor outcome, and that some of the cognitive symptoms could be ameliorated with proper treatment of post-TBI depression.

It has been hypothesized that depression may lower a person's incentive to participate in rehabilitation (Pagulayan, et al., 2008). Wade et al. (1998) found that a short, early psychological intervention post-TBI was related to significantly lower intensity and number of symptoms, and better rehabilitation outcomes. Treatment of co-morbid depression often lowered disability levels (Bombardier et al., 2010).

Knowing which groups are at higher risk for negative outcomes post-TBI would allow the most efficient use of intervention resources. Many of the studies on outcomes post-TBI in seniors have focused on the more severe forms of TBI. Rapoport et al. (2003a) suggested an investigation into whether or not a range of levels of TBI, including mild TBI, was related to an increased risk of depression in seniors. While the authors suggest that the literature to date does not establish that old age is a risk factor for increased incidence of depression post-TBI, Levin et al. (2005) did find old age was a predictor of major depressive episodes at three months post-

TBI. They suggested that the importance of age may have been masked in previous studies by the inclusion of other disorders such as substance abuse, which are more common in lower age groups.

Stonnington (2001) noted the importance of conducting more research comparing outcomes in those with TBI with and without depression, in order to better identify where early intervention could be most effective. Stonnington believed early intervention could help break the "feedback loop of depression causing low (post-TBI) functioning and low functioning causing depression" (pg.61). The author noted that once this pattern is established post-TBI, treatment becomes more difficult. Without psychological intervention, poor coping strategies used pre-TBI continued post-TBI. Bombardier et al. (2010) concluded that depression in TBI was "An invisible disorder often associated with an invisible injury; (therefore) aggressive efforts are needed to educate clinicians" (p.1944). Levin et al. (2005) stressed the importance of using brief screening one week post-TBI as depression post-TBI often went almost 6 months before treatment began (Levin et al., 2005).

Work with seniors has suggested that although TBI represents an increased risk of depression, most work has involved more severe forms of TBI (Raporport & Feinstein, 2001). It is of interest in this study whether milder forms of TBI (concussion, skull fracture) are found to put seniors at increased risk of post-TBI depression.

Chronic Pain. Chronic pain (CP) is also an important biopsychosocial issue associated with TBI. In the past, CP has been viewed mainly from a biomedical perspective. However, current understanding of mind-body interactions, coping styles, and the importance of psychosocial support, has stressed the value of viewing the origin, maintenance, treatment, and experience of CP from a more holistic biopsychosocial perspective (Gatchel & Turk, 1999). The

International Association for the Study of Pain (IASP) definition of pain includes biological as well as psychosocial aspects. According to the IASP definition, pain is "...[a]n unpleasant sensory and emotional experience associated with actual or potential tissue damage and described in terms of that damage" (Merskey & Bogduk, 1994). Gould et al. (2011) noted that CP has a complex relationship with other psychological disorders in TBI, and emphasized that pain "should be considered when investigating the relationship between psychological disorders and outcome, however the majority of studies have not done so" (p. 85). No other study, to date, has been able to prospectively look at CP pre-TBI and how it relates to outcomes.

CP is not uncommon in the elderly and the risk increases with age, with 24-75% of seniors in Canada reporting CP, with estimates increasing in recent years (Kraus & MacArthur, 1996; Range-Morin, 2008). This is often overlooked as a cause of falls or TBI, and pain in the elderly is often missed or undertreated (Leveille, et al., 2009; Ramage-Morin, 2008; Tai-Seale, Bolin, Bao & Street, 2011). CP is also related to other psychological factors that play a role in TBI, including sleep disturbances and depression (Shega et al., 2012). Shega et al. (2012) found that greater levels of pain were associated with higher levels of frailty, and suggested that persistent pain makes seniors significantly more likely to develop frailty. In support of this, Kroenke, Jianzhoa, Oxman, Williams and Dietrich (2008) found that pain interference and depression often coexist (42%) and amplify each other, with pain having a negative impact on the treatment of depression. Patients with the highest pain levels showed the poorest response to depression treatment at follow-up. Patients whose depression did remit showed an improvement in pain interference. Once again this suggests that many of these variables should be considered jointly when investigating frailty in the elderly.

CP may act as a risk factor for falls and TBI on its own, through functional decline and comorbid diseases, or through the medications associated with it. The use of analgesics has been thought to play a role in falls, but the evidence is contradictory. Levielle et al. (2009, p. 2218) found "no interaction between musculoskeletal pain and daily use of analgesics in relation to falls". The authors followed community-dwelling elders with CP and compared their subsequent fall rates. Over 60% of cases reported CP in one or more sites, and those with CP had a higher rate of falls compared to those without. There was a strong temporal relationship between severe pain in the previous month, and a 77% increased risk of fall in the subsequent month. The authors concluded that "Pain may be a marker for underlying pathology or treatments that could contribute to falls... possible mechanisms (including) central mechanisms, whereby pain interferes with cognition or executive function" (Leveille et al., 2009, p. 2219). Pre-TBI pain has also been found to be an independent risk factor for post-TBI depression, over and above demographic variables and litigation status (Bay & Donders, 2008). "Daily discomfort may accompany not only difficulties in performing daily activities, but also may be a risk factor for falls and fall-related injuries in the older population" (Leveille et al., 2009, p. 2220).

When calculating a health-adjusted life expectancy, Wolfson (1996) concluded that, in Canada, pain was second only to sensory problems in its effect on health-adjusted life expectancy. In the research conducted here, it is hypothesized that pre-TBI CP will be linked to worse outcomes including shorter post-TBI survival time. Pain post-TBI may lead to lower activity levels, greater functional decline, and an increase in psychological issues such as insomnia and depression.

Since falls are the most common cause of TBI in the elderly, risk factors for falls will be important to take into account. Leveille et al. (2009) followed 749 community-dwelling mobile

elders over 70 years of age with CP in none, one, or multiple sites, and compared their subsequent fall rates. Pain was measured by severity, number of locations, and the extent to which it interfered with daily activities. Drug use was also measured. Over 60% of participants reported CP in one or more sites. CP was associated with depression, osteoarthritis, and rheumatoid arthritis. Participants with CP had a higher rate of falls compared to those without chronic pain ($p < .05$). Each measurement of chronic pain (sites, severity, and impairment) was independently associated with falls, even after adjusting for previous falls and mobility function. This risk of falls increased with pain at more than one location, with the exception of back pain which did not increase risk of falls. There was also a strong temporal relationship between severe pain in the previous month, and a 77% increased risk of falling in the subsequent month. The authors were unable to control for depression as it was highly correlated with pain levels.

The authors concluded that "Pain may be a marker for underlying pathology or treatments that could contribute to falls... possible mechanisms for the pain-falls relationship can be grouped into 3 categories: local joint pathology, neuromuscular effects of pain and central mechanisms, whereby pain interferes with cognition or executive function" (Leveille et al., 2009, p. 2219). By neuromuscular effects the authors are referring to slowed response times, muscle weakness due to pain and inactivity, and possibly gait changes due to pain. Cognitive effects, such as pain as a distractor, may increase the risk of falls. There is less evidence for local joint pathology such as osteoarthritis.

CP is also a common outcome post-TBI. In a follow-up study of 132 subjects post-TBI over 8 months, 52-58% of participants were found to report CP. The incidence of CP increased with the severity of the TBI experienced (Lahz & Bryant, 1996). The authors noted that studies relying on self-report or doctors' records may underestimate CP in this population due to poor

self-monitoring in those with more severe forms of TBI. In a study of 146 participants undergoing inpatient rehabilitation, Hoffman et al. (2007) found the strongest predictors of post-TBI pain to be depression and female gender, while injury-related factors were no longer significant.

In a prospective data-linkage study (n=5853; Torrance, Lee & Smith, 2010), CP was found to be related to a higher rate of all causes of mortality. Data gathered from a health questionnaire was linked to death registries 10 years later. The authors noted that while some studies had been done on specific types of pain and mortality (e.g. cancer, cardiac) there were fewer and less conclusive studies in the area of CP. Participants were divided into mild and severe CP, with patients with severe CP showing shorter survival times than those with mild or no CP. Most of these results remained significant after adjusting for social economic status. The authors found the presence of CP was related to age, sex and education level. While this study is instructive, the population used is much younger than that investigated in the present study, and the increased risk CP puts on those post-TBI was not investigated.

Insomnia. Insomnia tends to increase with age, and is more common in women than in men (Cochen, 2009). Insomnia is a common problem post-TBI, with some studies suggesting that up to 42% of people report sleep issues post-TBI (Fogelberg, Hoffman, Dikmen, Temkin & Bell, 2012). Insomnia itself is related to lower QOL, and higher levels of dependence on others. In their sample of inpatient acute rehabilitation post-TBI subjects, Folgelberg et al. (2012) found that insomnia was strongly related to depression (R=.72), pain (R =.56) and anxiety (R=.39). It is proposed here that, in the frail adult, these comorbidities feed into each other creating increasing levels of problems. It will be important to examine the relationship of these variables to TBI and its consequences in the older adult. These relationships may suggest important areas where the

hypothesized feedback loop may be altered. For example it has been established that in the frail elderly, one path to insomnia is through long- term painful conditions (Cochen et al., 2009). Depression and anxiety are also significant risk factors for insomnia, and it is expected that all these variables will be related (Cairney, Corna, Veldhuizen, Hermann & Streine., 2008; Cochen, et al., 2009).

One of the issues with studies to date has been the reliance on self-reported problems. Part of the reason for this has been the lack of a specific ICD-9 code available for insomnia. As far as is known, this is the first study to examine these relationships using pharmacy data in an elderly population.

Risk Factors for Falls and TBI

Previous falls/TBI. The strongest predictor of a future TBI is whether or not a person has had a prior TBI (Bischoff et al., 2003). Annagers, Grabow, Kurland and Laws (1980) found that each TBI sustained put a person at increased risk for a subsequent injury. In fact, those over age 25 with a TBI were five times more likely to experience another injury than those without a previous TBI (Annagers et al., 1980). Falls themselves are a leading cause of TBI in the elderly, particularly among the oldest (Satariano, 2006). Wong et al. (1993) found that in a TBI rehabilitation population, males (7.4%) were more likely than females (4.5%) to report a previous head injury, and that reporting a previous TBI was associated with a history of alcohol use.

Previous falls in seniors are also linked to the development of both fear of falling and depression (Sjosten, Vaapio & Kivela, 2008). These conditions are associated with activity restriction and impaired physical functioning, which in turn increase the risk of subsequent falls.

Therefore many fall prevention programs are now including self-rated fear of falling as an outcome measure.

Other comorbidities. Gowing and Jain (2007) suggest that both medical and psychological co-morbidities in the elderly may predispose seniors to trauma. One study reported that 73% of seniors reported a co-morbid condition before their TBI vs. 28% of younger adults (Thompson et al., 2006). Amacher and Bybee (1987) found that 75% of cases of TBI in older seniors (>80 yrs) were associated with other co-morbid conditions or medications. The most common finding was antihypertension medication usage, followed by postural dizziness. In third place were myocardial infarction and previous stroke. Also associated were diabetic neuropathy, hip disease, Parkinsonism, and organic brain syndrome (Amacher & Bybee, 1987).The authors also suggested that history of cardiac arrhythmia, postural dizziness, chronic hypolvolemia (low blood volume), and hyponatremia (low blood sodium levels) would predispose seniors to falling. Strang, McMillan and Jennett (1978) found that 75% of cases of TBI due to falls in seniors could be traced back to a predisposing condition (including cerebrovascular episodes in 17% of cases).

Wilson, Pentland, Curet and Milller (1987) retrospectively investigated possible contributing factors leading to TBI in the elderly in a neurotrauma unit. They found that postural or orthostatic hypotension was present in 22.2% of the cases for which they could get data, hearing impairments in 24.1% of cases, and visual impairments or epilepsy in 6% each of cases. Orthostatic hypotension is a drop in blood pressure leading to dizziness when moving from a seated position to standing, and has many causes including diabetes, brain aging, low cardiac output and medications such as sedatives, antidepressants and antihypertensive medications (Rubenstein, 2006). Mental impairment was another important predisposing condition, present in 20.3% of those studied. Ziere et al. (2006) conducted a cross-sectional analysis of polypharmacy

and falls in seniors. The authors found that conditions associated with falls in seniors included: Parkinson's disease, stroke, depression, hypertension, hypotension and diabetes.

Medications and polypharmacy. The most accepted definition of polypharmacy is the use of three or more medications. LeBlanc et al. (2006) and Abelson-Mitchell (2008) suggest that polypharmacy and side effects of medications play a role in the increasing number of falls leading to TBI seen in the elderly. Polypharmacy has been found to increase the risk of falls in seniors (Ziere, et al. 2005). In Ziere et al.'s (2005) study, more than 20% of seniors met their definition of polypharmacy. Ziere et al. (2005) used a cross-sectional design whereby nearly 7,000 seniors in the Netherlands were assessed by interview for polypharmacy and fall history. Their fall rates for the previous year were also investigated. Those with dementia or who were unable to give a fall history were excluded from the study. It was hypothesized that polypharmacy itself was not an independent risk factor for falls, but rather that the use of fall-risk-increasing drugs led to a higher rate of falls among seniors taking multiple medications. The authors (2005) found 28 drugs associated with an increased risk of falling after controlling for gender, age, comorbid conditions and disabilities. Risk-increasing drugs included "central acting antiobesity products, calcium preparations, potassium sparing diuretics, oxicams, quinine and derivatives, anilides, anxiolytics-benziodiazepine derivatives and hypnotics-benziodiazepine derivatives" (Ziere et al., 2005, p. 219). Interestingly, women were more likely to be using risk-increasing drugs than men, which may be a factor in the increased rate of falls in females. While fall risk increased significantly with the number of drugs used daily, polypharmacy was only an independent predictor of falls when one of the drugs taken was a risk-increasing drug. There was also a dose-response function where the odds ratio (OR) of falling increased from 1.4, when taking three medications, to 1.6 for four or more medications ($p<.01$). When a patient was taking

a risk-increasing medication OR for a fall increased from 1.3 for one medication to 2.5 for two medications (P<.001).

Whether it is the co-morbidities themselves or the polypharmacy associated with them that lead to an increased fall risk in seniors is an area of some debate. In a meta-analysis, researchers came to the conclusion that it was the comorbidity rather than the medications that explained the increased risk of falls (Leipzig, et al., 1999).

Studies have suggested that benzodiazepines, especially long-acting ones, put seniors at a greater risk of falls and fall-related injuries (Ray, Puruhottam & Gideon, 2000). Ray et al. (2000) found that use of benzodiazepines was associated with a 44% increase in risk of falls, after controlling for other medications such as those for anti-Parkinsonism, anticonvulsants, and anti-hypertensives. The risk of falls increased with dose, and also with the initial start-up on benzodiazepines. However a recent study looked at the risk of falls in a susceptible population: frail elders in a geriatric acute care facility. Gauber-Dahan et al. (2011) found that risk was only substantially increased for elders on both a benzodiazepine and neuroleptic.

The use of analgesics is sometimes thought to play a role in falls, but the evidence is contradictory. While pain was significantly related to falls, Levielle et al. (2009) found no relationship between daily use of analgesics and falls. In fact, a previous study by the same author noted that females with pain who were analgesic users had a lower rate of falls than females without pain who were not analgesic users (Levielle et al, 2002). Levielle et al. (2002) followed a group of 940 women with musculoskeletal pain over three years as part of the Women's Health and Aging Study. Moderate to severe pain put women at increased risk of falls compared to low levels of pain. This risk was attenuated somewhat, however, if the pain was treated with daily analgesics. In further support of untreated or undertreated CP as a risk factor

for injuries, Voaklander et al. (2006) found that farmers who had stopped taking narcotic pain killers in the preceding 30 days were at increased risk of sustaining a farm injury. The authors suggest that the pain itself may play a role in increasing risk of injury.

Antidepressant medication use has also been linked to falls in the elderly (Thapa, et al., 1998). It was hoped that newer antidepressants such as selective serotonin reuptake inhibitors (SSRIs) would decrease the risk of falls and injuries compared with tricyclic antidepressant use, which is known to leave seniors vulnerable to orthostasis and psychomotor impairment. Thapa et al. (1998) conducted an inception cohort study, comparing the rates of falls in over 2000 nursing home residents who were new to using either SSRIs or tricyclic medication. They found that both types of antidepressants increased the risk of falls and injurious falls, once adjustment was made for baseline factors. While tricyclics showed the strongest relationship with falls, both SSRIs and tricyclic medications increased the risk of both falls and injurious falls compared to the risk found for non-users, and the risk increased with dose (RR= 2.0, 1.3). These effects remained after taking into account demographic variables, cognitive impairment, level of independence, previous falls, co-existing illnesses, and other medications such as anti-convulsive and anti-Parkinsonism medication, anti-psychotics, or other sedatives. The increased risk remained during the 180 day follow-up. However, this study population was confined to a nursing home and composed of frail elderly subjects.

Although the type of antidepressant taken did not increase the risk of falls in new cases, risk of falls was affected by the reason they had started using the medication, and other drugs used. Depression is a common reason for using antidepressants, but it is by no means the only impetus. Other purposes include treatment for anxiety or insomnia (antidepressants act as hypnotics at low doses), and behavioural problems associated with dementia. Thapa et al. (1998)

found that 74% of cases starting on SSRIs were using them for depression, and 55% of those using trycyclics were using them for depression, while 34% of seniors started on trycyclics in the study were using them for behavioural problems associated with dementia. While dementia itself may be a risk factor for falls, those who started either type of antidepressant for behavioural problems associated with dementia showed a higher rate of falls compared to those who started antidepressants for depression.

An interesting interaction was also found between the use of trycyclic antidepressants and the use of cardiovascular medications. Elders taking three or more cardiovascular medications in conjunction with trycyclic antidepressants showed a RR of 3.3 for falls vs. 1.8 for those on trycyclics without cardiovascular medications. The same results were not found for those using SSRIs (Thapa et al., 1998).

While Thapa et al.'s (1998) study was prospective, it does not prove causality. Was it the depression or the antidepressants that led to an increased risk of falls? The medication can cause increased postural sway, psychomotor impairment, and orthostasis. However, there are also ways that depression itself could be associated an increased risk of falls. Depression tends to increase along with disability levels, and therefore may be acting as a proxy measure of disability or a decline in mental or cognitive health. Depression is associated with psychomotor impairment and decreased activity. With decreased activity levels, seniors tend to become decompensated much more quickly than their younger counterparts (Thapa et al., 1998). In support of this, Stuck et al. (1999) found depression to be strongly related to risk for decline in functional status. Ziere et al. (2006) also found that depressive episodes were related to an increased risk of falls in seniors.

Vitamin D deficiency and insufficiency. Canadian studies have found a high prevalence of vitamin D deficiency in the adult population. This deficiency has recently been argued to play a role in osteoarthritis, muscle weakness, depression, falls, disability, and CP, all of which are linked to TBI in the elderly (Chang et al., 2010; Dawson-Huges, & Josse, 2009; Rucker, Allan, Fick & Hanley, 2002). Seniors, especially in Canada, may be at risk of vitamin D insufficiency as there are few months in the year where vitamin D can be synthesized from sunlight due to the northern location. In Boston, adequate vitamin D cannot be synthesized from sunlight from November through February, while in Calgary this occurs from October through March (Dawson-Huges, & Josse, 2009).

Vitamin D deficiency can be defined as 25- hydroxyvitamin D <40 ng/ml. Vitamin D insufficiency or preclinical vitamin D deficiency (inadequate levels for bone health) has been receiving more attention (Rucker et al., 2002). The level of vitamin D that is considered insufficient is currently under review, and some authors have proposed therapeutic levels as high as <80 nmol/L (Rucker et al., 2002).

Rucker et al. (2002) randomly selected 168 participants in Calgary from an ongoing population-based study of osteoporosis, and tested their vitamin D levels over a three month period. Vitamin D levels were obtained from the participants every month. The authors found that, using the most conservative definition, 34% of participants were vitamin D deficient at some point during the study. Using a higher level (50nmol/L), 61% met the criteria for vitamin D insufficiency at some point during the study, and using the new proposed cut-off of 80nmol/L, 97% of Calgarians studied had vitamin D insufficiency at some point. The authors concluded that this high prevalence warranted dietary supplementation, especially in the elderly (Rucker et al, 2002).

Langlois, Greene-Finestone, Little, Hidiroglou and Whiting (2010) found that 68% of elders had serum D levels below 37.5 ng/mL. Rucker et al. (2002) reported that increased age was associated with lower vitamin D levels, and Bischoff-Ferrari et al. (2004) found that 90% of elderly women from an institutionalized population were vitamin D deficient. Low vitamin D levels in the elderly may be due to fewer outdoor activities, as well as the fact that seniors synthesize less vitamin D in the skin when exposed to light (Chang et al., 2010). Low vitamin D levels are associated with an increased risk of developing frailty as well as frailty itself (Topinkova, 2008).

Vitamin D treatments are associated with improved musculoskeletal function with regard to muscle weakness and falls (Bischoff et al., 2003). Since vitamin D is synthesized in the skin, vitamin D deficiency also varies with skin pigmentation. Those of European descent tend to be at a lower risk for vitamin D deficiency than those from other areas (Langlois et al., 2010). Vitamin D deficiency in females over 70 years of age was found in 28.5 % of Caucasians, 55% of Mexican-Americans, and 68% of non-Hispanic African-Americans (Dawson-Huges, & Josse, 2009). Vieth, Cole, Hawker, Trang and Rubin (2001) also found that, in a Canadian sample, only 14.8% of Caucasian women were vitamin D insufficient (<40nmol/L), while 35.6% of non-Caucasians were found to have insufficient levels. Studies indicate that the prevalence of low vitamin D has increased since 1994, possibly due to increased obesity, less consumption of vitamin D-supplemented milk products, and increased use of sunscreen (Dawson-Huges, & Josse, 2009). It has also been suggested that poorer nutrition, including low vitamin D levels, is more common in urban vs. rural settings (Kannus et al., 1996).

Both Mesrine, Boutron-Ruault and Clavel-Hampton (2010) and Wilber, Sullivan and Caramango (2010) argue that vitamin D may mediate the association between chronic pain and

increased risk of falls in the elderly found in the study by Leveille et al. (2009). Low vitamin D is associated with an increased risk of falls, muscle pain, and with multiple-site pain, and may lead to an increased risk of falls through increased muscle weakness. In response, Leveille, Kielly and Kiel (2010) re-analyzed data taking into account vitamin D or multivitamin supplementation, and found that supplementation was not associated with CP. However, they had no measure of vitamin D levels (supplementation may have occurred due to a finding of low levels), and dosages associated with improvements of low levels of vitamin D are higher than standard dosages (Bischoff-Ferrari et al., 1999).

In a recent Statistics Canada study which ran from 2007-2009, it was suggested that males were more likely to have a vitamin D deficiency than females (Langlois et al., 2010). This study failed to show, however, if this pattern holds in the elderly. Contradictory evidence comes from an American study where only 11% of males older than 70 were classified as vitamin D deficient, while 16.5% of females older than 70 met the criteria for vitamin D deficiency (Dawson-Huges, & Josse, 2009).

Bischoff et al. (2003) investigated whether treatment with vitamin D and calcium vs. vitamin D alone would reduce falls in elderly women in long-term care. Participants in the double-blind randomized trial received either vitamin D alone or vitamin D with calcium over a period of 3 months. Fall rates during the pre-treatment period were then compared to falls during treatment. Treatment with both vitamin D and calcium led to 62% fewer falls, and "reduced the risk of falling by 49% compared with calcium alone" (Bischoff et al., 2003, p.343). Vitamin D supplementation was also associated with improvements in musculoskeletal functioning. This was after controlling for previous falls, baseline vitamin D levels, and age. The authors went on

to suggest the use of vitamin D in fall prevention programs as it seemed especially effective in preventing tumbles in recurrent fallers.

This result is in line with a meta-analysis by Bischoff-Ferrari et al. (1999) in which a significant reduction in fall rates in seniors was seen with vitamin D supplementation, ranging from two months to three years. Vitamin D supplementation led to a 22% decrease in the OR of a fall with a NNT (number needed to treat) of only 15. This means that one would only need to treat 15 seniors to prevent one fall. There were an insufficient number of studies at the time to determine difference by gender, baseline vitamin D levels, or supplementation level. Sato, Iwamoto, Kanoko and Satoh (2005) randomly assigned 96 female elders with post-stroke hemiplegia to either vitamin D supplementation or placebo, and then followed them for two years. Vitamin D supplementation was associated with an increase in muscle strength and a 59% reduction in falls.

In summary, a review of the existing literature on the antecedents and consequences of TBI in the elderly suggests that a wide range of interdependent factors are involved, many of which can be seen in figure 1. This includes factors such as psychological disorders (including depression, insomnia, and CP) which increase risk of both TBI and poor outcomes post-TBI, as well as physical factors like previous falls, medical disorders, polypharmacy, and vitamin D deficiency which also expand the risk of falls and TBI in an elderly population.

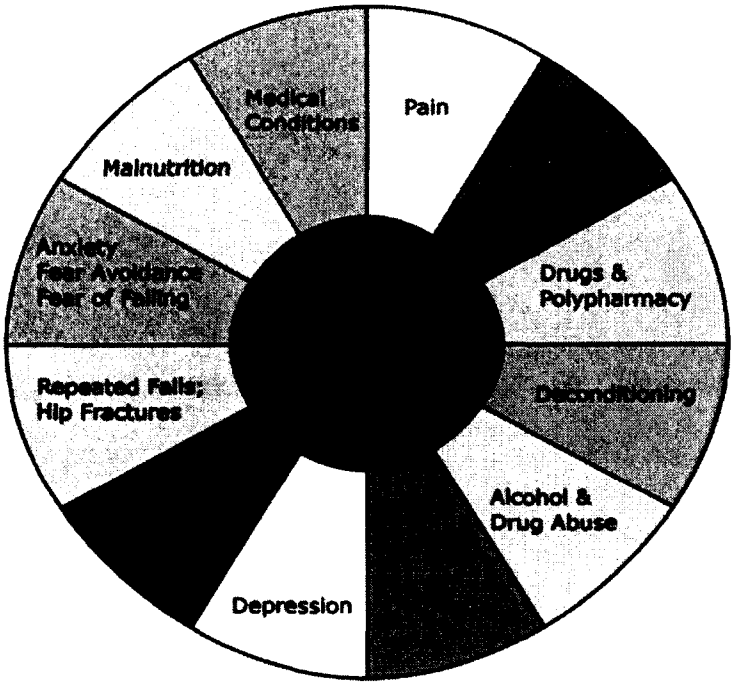


Figure 1: Risk factors associated with traumatic brain injury in seniors

Hypotheses and Research Questions

This research addressed the foregoing model by evaluating the following hypotheses and research questions.

Survival analyses. It was hypothesized (hypothesis 1) that cases with CP prior to TBI would show shorter survival times post-TBI than those without pre-TBI CP, regardless of gender. Analyses controlling for cancer pain were also undertaken.

Risk of depression post-TBI. It was hypothesized (hypothesis 2) that cases would be at higher risk of post-TBI depression than controls during the same time period. Analyses were undertaken for all cases of depression within one year post-TBI, as well as new incidences of depression within one fiscal year post-TBI. These same relationships were also examined

specifically in cases with milder TBI only. It was hypothesized that even in cases of milder TBI there would be a significantly increased risk of depression (hypothesis 2b).

Characteristics of pre-TBI CP. Is there a profile of characteristics that distinguishes cases with CP prior to TBI from those without? It was hypothesized that those with prior CP would show a higher level of prior co-morbidities such as depression, anxiety, and insomnia (hypothesis 3).

Risk factors associated with post-TBI depression. What psychological and demographic factors are related to the post-TBI risk of depression (research question 1)? Logistic regressions will be undertaken to investigate this pattern in cases with depression within one fiscal year post-TBI, as well as new cases of depression post-TBI specifically.

Predicting post-TBI CP. What psychological and demographic factors predict the development of post-TBI CP in cases (research question 2)? Logistic regression will be undertaken to investigate these relationships in CP developed within one fiscal year post-TBI.

Methodological Issues

Research with elderly. There are some special considerations when one is conducting or using research based on the elderly, and in particular when researching TBI. One factor is the challenge of obtaining a representative sample. If one relies entirely on hospital records, two important groups will be left out. Those who expired before reaching the hospital will not be accounted for, along with those whose head injuries were less serious, and who perhaps opted to visit their family doctor rather than an emergency room. For this reason it is important to have more than one source of information.

Another question is which group to use as a control group. There is some disagreement over what type of control group is the most appropriate. For example, when studying seniors and

TBI, at least three possible control groups can be proposed: 1) seniors without TBI (to study how TBI effects outcome, etc.), 2) younger groups with TBI (how does the effect of TBI change with age?), and 3) seniors with some other medical condition (such as arthritis). This last group would be meant to control for confounding due to non-brain related injuries that could affect functioning/outcome (Rapoport & Feinstein, 2000).

The measurement of severity of brain injury may be more difficult in some elderly patients. If the patient has intellectual impairments, it may be difficult to measure post-traumatic amnesia, and administer other tests necessary to assess brain injury (Selman & Benzel, 1999).

Old age itself produces an increased risk of decreased functioning or death. This can confound studies that look at long term survival of seniors compared to younger age groups (Flaada et al., 2007). One way to allow for this is to use dummy variables in the analysis that take into account predicted lifespan based on actuarial tables and gender. Studies that have used this method have noted that seniors did not necessarily show a large increased risk of death post-TBI (Flaada et al., 2007).

The overriding issue that distinguishes illness in older adults from that of young or middle-aged adults is the increased complexity of characterizing health status. Measuring and understanding this complexity of health status in epidemiology is a considerable challenge. "This complexity derives from several sources: the presence of multiple chronic diseases, the increased risk of ill health associated with common environmental challenges, the higher proportion of persons at risk for adverse outcomes of diseases and their treatments, and the physiological changes that come with increasing age" (Wallace & Woolson, 1992, p.11).

Strengths of administrative database analysis. The detailed use of pharmacy billing data in addition to International Classification of Diseases (ICD) coding, a health problem

classification system used in health billings/studies in Canada and worldwide in identifying anxiety, insomnia, depression, and CP is unique to this study. The use of pharmacy data allows never-seen-before precise interpretation of Drug Identification Numbers (DIN, present on any prescription/over the counter drug sold in Canada). Exacting conservative pharmacological criteria were set for CP, depression, insomnia, and anxiety, before and after TBI, with help of both a family physician pain specialist and a geriatrician with an interest in pain. These were then used along with ICD-9 codes in identifying cases. All ICD-codes or DIN-codes used were divided into either pre- or post- TBI.

Little research has been done using multiple database types when looking at psychological variables in relation to TBI. A recent Canadian publication made a plea for studies not relying solely on hospital data, but rather using multiple sources (**Tannenbaum, Lexchin, Tamblyn, & Romans, 2009**). Hospital data alone does not shine any light onto psychological factors such as depression, insomnia, or CP in TBI. This dissertation combines doctors' billings, hospital data, and pharmacy data from 1991-2007, to get the most complete picture of TBI in seniors in Canada thus far. This study will examine the outcomes post-TBI in cases with prior CP, as well as looking at depression as an antecedent and outcome of TBI. Pharmacare data contains information on all reimbursable prescriptions between 1991 and 2007, while the Medical Services Payment Plan File (MSP) is a database of billings submitted by health care providers in British Columbia. The hospital database contains records of all hospitalizations in British Columbia.

The availability of both pre-TBI data and a long period of follow-up is a great asset to this study. Most studies looking at pre-morbid conditions and TBI have relied on self-reported psychological conditions, and have had a sole focus on one psychological disorder, making it

difficult to look at the relationships between them. There has also been no means to control for CP in analyses (Gould et al., 2011). The epidemiological nature of this study allows access to long-term administrative information on multiple psychological disorders. This unique approach is one of the greatest strengths of this study, as it facilitates answering questions that cannot easily be looked at in other ways, and can identify important areas for follow-up. As far as is known, no study thus far has had non-self-report information on pre-existing depression, anxiety, insomnia, and CP together when investigating outcomes in TBI, nor have studies looked at this combination of psychological variables with an extensive period of follow-up time available. This study will help to fill in these gaps in the research.

This analysis will produce a more accurate estimate of TBI than research relying on one point of entry to the health system. Estimates of TBI often include only hospital cases, leading to underestimation (Rapoport & Feinstein, 2000). Studies that use only one point of contact within the medical system (death records, practitioner data, hospital data) will underestimate TBI incidence more than those that use more than one data source (Corrigan, Selassie & Orman, 2010). For example, in the United States, hospitalized TBIs include only 20% of total cases (Corrigan, Selassie & Orman, 2010). Linking multiple databases enables the investigation of psychological disorders within the TBI population using information that would not have been available using only the hospital information. A Canadian study found that seniors were most likely to go to their general practitioner for psychological issues (Hardy, Kelly & Voaklander, 2001). Palin, Goldner, Koehoorn and Hertzmann (2012) argued that general practitioners are "The main, or often the only, source of mental health care for most Canadians, and are typically the gatekeepers to specialty medical care" (p. 367).

The fact that in the present study it will be possible to link datasets and remove duplicate TBI cases is also a great strength. Not all past research has been able to effectively do this (Picket, Kelly & Simpson, 2004).

Epidemiological analysis of TBI provides data that are useful for identifying injury patterns, as well as high-risk groups (Pickett, Simpson & Brison, 2004). A prospective cohort study is beneficial, as a temporal association can be demonstrated between TBI in seniors and multiple outcomes, as well as in calculating risks associated with pre-morbid conditions. One of the strengths of this study is the availability of a large number of cases, allowing us to study relationships and patterns that might have been impossible with smaller datasets (Pickett, Simpson & Brison, 2004).

Limitations of using health data. A remaining issue is that this analysis will only capture cases who presented for medical treatment at some point in time. There will be a subset of seniors that do not present for treatment or mention depression or other psychological issues, and these will be missed in this analysis (Butler, Cohen, Lewis, Simmons-Clemmons & Sunderland, 1997). Sambamoorthi, Walkup and Akincigal (2003) noted that the elderly were less likely to receive treatment for their depression than younger populations. In the elderly it is common for depression to be associated with high levels of comorbidity, making awareness and identification of depression in this population all the more difficult (Charlson & Peterson, 2002).

II. Methods

This study used a historical cohort design to examine the effects of psychological factors such as depression, CP, and anxiety in cases of TBI in seniors aged 65 years and over in British Columbia. This section will discuss the datasets and software used, major variables, and the selection of cases and controls.

Apparatus and Materials

Datasets. All databases used cover the years 1991-2007. All three databases were provided for both the cases and the control group. These datasets were obtained as part of a larger research project in progress at the University of Alberta School of Public Health. This dataset includes all British Columbia seniors who had a TBI during the fiscal year 1993-1994.

Pharmacare. This file contains the date of purchase, types of medications purchased, and the quantity of medication reimbursable under Pharmacare in British Columbia seniors. All residents of BC aged 65 years and older are eligible for coverage. This data was distributed by the Research Liaison Unit, Population Data BC as part of a larger research project through Don Voaklander at the School of Public Health, University of Alberta. As these files are used for billing, they are considered reasonably accurate.

Medical services plan payment file. This is a database of fee-for-service claims submitted by health service professionals in BC for of medically required services for seniors. In investigating general practitioners' use of mental health billing codes, high levels of sensitivity and specificity were found in comparisons to medical chart data (80.7%, 97%; Palin, et al., 2012). A three digit ICD-9 code is assigned to each encounter. This data was also distributed by the Research Liaison Unit, Population Data BC as part of a larger research project through Don Voaklander at the School of Public Health, University of Alberta.

Canadian Institute for Health Information (CIHI) hospital inpatient database. This is a record of all hospitalizations in BC seniors for the time period provided. Records are completed by individuals trained in their accurate creation. Data available includes admission and discharge dates, up to 16 ICD-9/10 diagnostic codes, up to 10 ICD-9/10 procedure codes, etc. This data was distributed by the Research Liaison Unit, Population Data BC as part of a larger research project through Don Voaklander at the School of Public Health, University of Alberta.

Software Used and Data Cleaning. All statistical analysis was undertaken using SPSS, using both menus and syntax. Case finding, the labeling of psychological disorders using the criteria created here, and the random selection of controls was done using AWK (see Table 1 in results for ICD-9 codes and a list of appendices for Pharmacare rules). Hospital and community files were merged. Only those subjects aged over 65 and with TBI within the time period from April 1993 to the end of May 1994 were selected. Complete data screening and cleaning was undertaken prior to analysis. TBI was defined by ICD-codes for concussion (850), head fracture (800-804), intracranial injury (851, 854) and intracranial injury with hemorrhage (852-853).

AWK is a powerful computer language used in working with large databases. AWK has many special features for handling text databases, like an input loop which runs the same program on every line in turn to make repetitive programs shorter, and a column splitter which makes finding column 5 as easy as 5$. Crucially, it has associative arrays for easy storage and recall of matching pieces of information (like whether a drug is in the set of drugs being looked for). But unlike special-purpose languages like SPSS and SQL, AWK is not restrictive -- larger, more traditional programs can be written in AWK when these tools aren't enough. See the AWK User's Guide for more information (Brennan, N., n.d.; http://www.gnu.org/software/gawk/manual/gawk.html).

AWK files were run in succession, creating and using associative arrays to identify cases of psychological disorders based on ICD-9 codes, drug DINs, quantities of drugs dispensed, dates between prescriptions etc. See Appendices A – D for a list of drug DINs and the criteria used to identify psychological variables. See Table 1 for a list of ICD-9 codes used in identifying psychological variables.

A program called Shuf.exe was used to select a random sample from the control group. This program uses a random seed to select a list of lines from a list of potential cases in random order. This long list of ID numbers was then easily stored and used in an associative array in AWK to search for participants within the drug, hospital and medical services payment plan files in conjunction with various criteria for psychological disorders.

Key Variables. Psychological variables such as depression, CP, insomnia, and anxiety were extracted both pre and post TBI using ICD-9 codes and pharmacy data. Substance abuse was explored but there were too few cases for analysis. Non-traumatic brain injury (e.g. ICD-9 434: Occlusion of cerebral arteries) was also explored. Demographic variables such as age at the time of injury and gender were also used.

Cases

This was a case control study of 657 cases of TBI with data from 1991-2007. The research covered cases of TBI taking place from April 1, 1993 to March 31, 1994; therefore two years of retrospective data are available as well as a long follow-up period.

Controls

The control group consisted of 3,000 randomly selected BC seniors (>65 years) who were not hospitalized for a fall or a fracture. Those with TBI codes were removed from analysis, as

well as anybody under the age of 65. Therefore the control group contained British Columbia seniors without a TBI.

AWK programming was used to select a set of controls who had codings during the same time period used to select TBI cases. The median coding date in that time period for each individual was selected as a marker separating 'before' and 'after' for comparisons with the cases (e.g. survival curves). A random sample of 3,000 controls was selected for this study as it has been suggested that there is little gained in going beyond 4 controls per participant (Grimes & Schulz, 2005). One recent study suggested that a 1:4 ratio of cases to controls was the golden standard to achieve a high level of statistical power (Pyo Hong & Wan Park, 2012).

Analytic Strategy

Depression and TBI.

Risk of depression post TBI. The pattern of incidence of depression after TBI in seniors within the first year post-TBI compared to those without TBI was investigated. Separate analyses were run for all post-TBI depression, and new cases of post-TBI depression. It was hypothesized that cases with TBI would show a higher risk of depression than controls (hypothesis 2). Any patterns identified were examined further with respect as to whether they were consistent when only those with mild to moderate TBI were compared to the control group.

Risk factors associated with post-TBI depression. A principle question under investigation was "what effect do psychological, demographic, and TBI variables have on the risk of developing depression post-TBI?" (research question 1). This was investigated using logistic regression analysis. In this analysis, post-TBI depression was the dependent variable of interest, while the suspected risk factors were the independent variables. Several different models were investigated: models predicting post-TBI depression with all available variables, models

that did not include pre-TBI depression, and models focusing on new cases of depression post-TBI.

Survival Analyses. Differences in outcomes between seniors with CP prior to TBI and those without prior CP were investigated using Kaplan-Meier (KM) and Cox regression survival curves. It is hypothesized that cases with CP will show shorter survival times (hypothesis 1) than those without CP. Separate KM curves were created for male and female CP cases. Survival curves controlling for cancer in the group with CP were created, and differences between CP cases with and without ICD-9 codes were investigated.

Predicting CP group membership. The profile of psychological and demographic variables distinguishing cases with CP prior to TBI from a control group of those without CP prior to TBI was also investigated. Logistic discriminant function analyses were used to identify potentially important variables in this relationship. It was hypothesized that CP patients would show higher levels of various psychological disorders (hypothesis 3).

Predicting post-TBI development of CP. Logistic regression analyses were also undertaken to investigate the relationship of post-TBI CP to pre-TBI variables such as psychological disorders and demographic variables (research question 2).

This is the first study of its type to include the use of both pharmacy data and general care data along with hospital data. The use of pharmacy data in identifying those with psychological disorders (e.g. depression) will allow for a more accurate and detailed look at these questions.

Logistic Regression analyses. It is expected that there will be significant correlations between some of the psychological variables used in the logistic regression analyses. With this in mind, backwards logistic regressions techniques were undertaken for these analyses. There are several compelling reasons for implementing the use of backwards format logistic regression in

the present analyses: 1) It has been suggested that a backwards format is applicable when there is not a hypothesis to guide variable selection as seen in Levin et al. (2005) and, 2) Several of the important variables used in this analysis are in correlated relationships, so that involving all variables may result in masking or underestimation of important relationships. Mernard (1997) suggests the use of backwards logistic regression in cases where a suppressor effect is suspected. In these cases a backwards model may be more powerful than a stepwise forward model in unmasking relationships that may be missed by other methods.

Multicollinearity may result in unstable beta estimates (Tabachnick & Fidell, 2001). With a positive relationship between many of the predictor variables, one may expect "coefficient flipping," where the relationship within the model is opposite in direction to what is seen alone, due to what is known as net or negative suppression occurring between the variables (Lancaster, 1999). This means that a variable may receive a negative Beta weight when included in a model with other related variables, while on its own it would show a positive relationship with the outcome variable (Lancaster, 1999). This is not due to the relationship to the variable being predicted, but to a relationship between the variables used within the prediction. This coefficient flipping is known as a Simpson's Paradox or the Yule-Simpson effect. In a Simpson's Paradox the relationships at the aggregate level are the opposite of what is seen when the data are examined with the groups separately. For example, Bickel, Hammel and O'Connell (1975) discussed this effect in relationship to admissions at Berkley University. When looked at overall, there seemed to be a strong bias in favour of male students. However, when the individual departments were examined, no such bias was found. In fact, many departments showed a small bias towards accepting female students. Simpson's paradox can occur due to relationships between the predictor variables (collinearity) or unknown third variables.

As it is not uncommon for the elderly to have more than one psychological issue, collinearity cannot be avoided here while still representing the general population. Chi-Square analyses will therefore be pursued to determine the direction of any relationships found in logistic regression, and extreme caution must be taken in interpreting any β's or odds ratios.

Use of Pharmacy Data in Identifying Psychological Disorders

This is a simplified explanation of the drug DIN criteria. For full details, see the appendices. Particular attention was paid to how these medications were used in practice in an elderly population in the early to mid-1990s. Insomnia medications fell under several criteria. First were medications either marketed only for, or used only in, insomnia in the elderly, as determined by the health professionals interviewed. In discussions with the doctors who helped create these criteria, it was apparent that most anxiolytics may also be used as hypnotics. If a standard dose was an anxiolytic three times daily, it was assumed that a twice daily dose represented use for anxiety (see Appendix A), while a third dose (as for a minimum dispense of 90 pills, three times daily) represented a sleep aid (see Appendix B). Hence coding tranquilizers for use as hypnotics was limited to those used three times daily. This was restrictive but thought necessary to avoid false usage cases. Otherwise, to meet the criteria as a case of insomnia, cases had to be using two different potential tranquilizing medications during the same time period. The health professionals believed this meant that while one prescription may be being used for anxiety, the other was very likely being used to actually treat insomnia. Finally, certain antidepressants are so sedating, that they would only be used as sleep aids and were additionally coded to reflect that (see Appendix B).

To meet the criteria for depression, cases had to be taking what was considered to be at least a semi-therapeutic dose for that particular antidepressant type. In this manner, some anti-

depressant DINs required a higher quantity dispensed before the participant qualified as a depression case (see Appendix C). There are some antidepressants whose only use is for depression and they were coded accordingly.

To meet the criteria for CP, cases had to show severe levels of pain as verified by their pattern of pain killer use, as well as prolonged pain as shown by painkiller use and/or musculoskeletal codes longer than a 3 month period (for specific pattern assessed see Appendix D). Opioids were coded as the highest level painkiller. Tylenol with codeine #3 and equivalent and Ketorolac were next. The next level included drugs equivalent to Tylenol with codeine #2. NSAIDs were coded as having lower level painkilling properties.

The use of antipsychotics was not dealt with. Some are sedating, some rarely used in sleep, and it was felt there would be no way of determining why they were being used. Therefore the prescription of antipsychotics was not used in any of the drug DIN criteria created in this study.

III. Results

Descriptive Statistics

Cases. Datasets merged include the hospital and community files for the time period from April 1993 to the end of May 1994, and subjects aged over 65 years of age with a TBI ICD-9 code were selected. This left 651 cases, 333 being female (52%) and 309 male (47%). The mean age was 77.7 (s d= 7.7). Ages ranged from 65 to 106.

Controls. The control group was made up of 3,000 participants: males=1292 (53.1%), females = 1676 (55.9%). The average age of the controls was 73.70 (sd = 6.47, range: 65.0-103.3). Chi-square analysis failed to find a difference in gender ($\chi^2 = 3.68$, $p>.05$) between the two groups. The control group was on average 4 years younger than the participants (T = 14.04,

p<.001. C.I = 3.50-4.64), a small difference magnified by the power of a large sample. However, the standard deviations of the controls and participants were 6.47 and 7.68 respectively.

Age distribution and incidence rates. The age distribution by gender of the cases is represented in Figure 2. There were more females than males in the older age groups (ages 80-89) with the exception of the oldest old, where the numbers were similar (22 vs. 24). Low numbers in the oldest old mean that the power to find differences by age group in this group will be diminished.

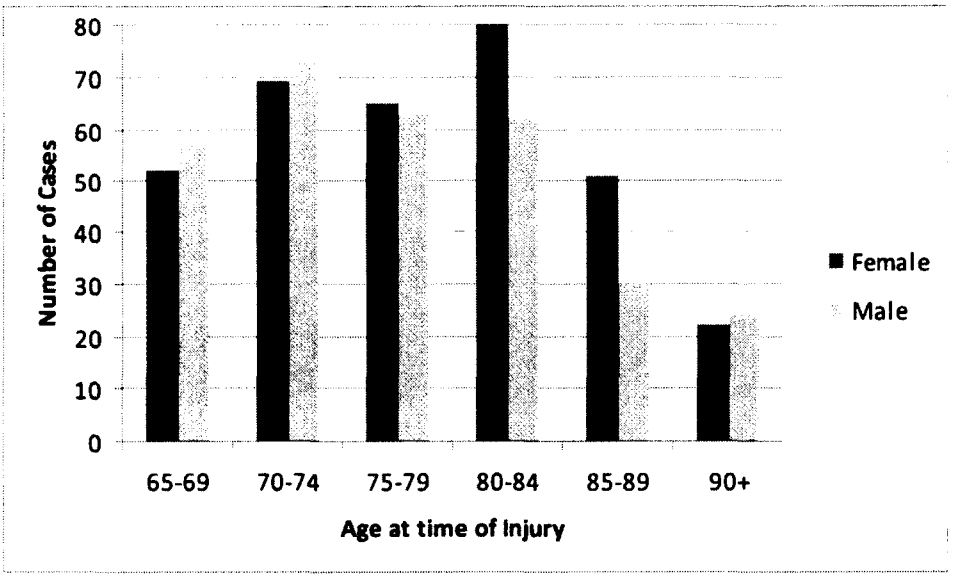


Figure 2: Number of cases by age group and gender

Using population estimates for 1994 from BC Statistics, the incidence of head injuries for the fiscal year 1993-1994 for each gender was estimated (http://www.bcstats.gov.bc.ca/data/pop/popstart.asp ; See Figure 3)

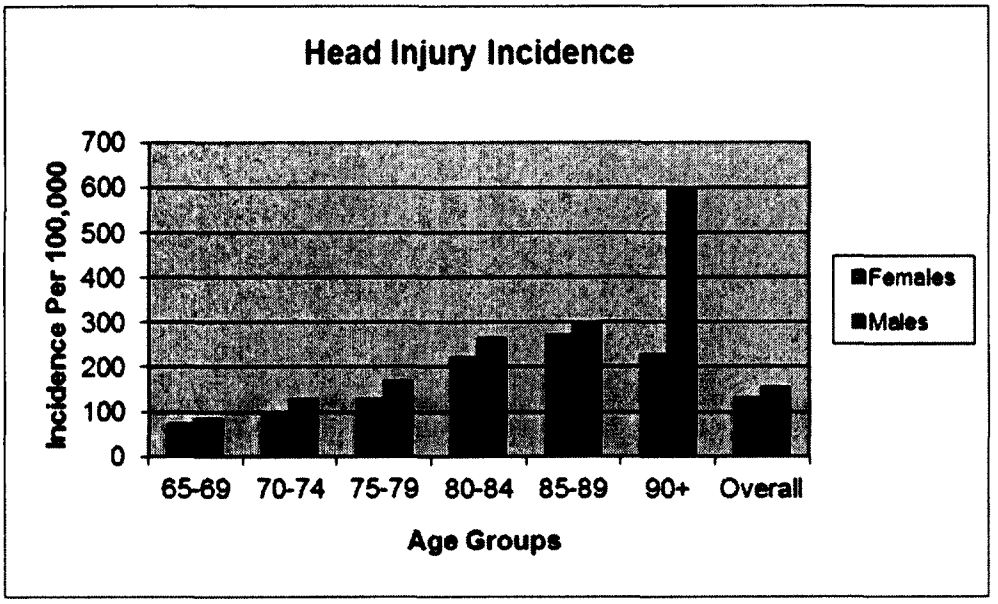


Figure 3: Traumatic brain injury incidence rates per 100,000 by gender

The overall incidence of TBI per 100,000 was 128.88 in women and 152.86 in men. The incidence of TBI increased with age, and was generally higher in males than females. This may be due to the near equal number of males and females present in the oldest age group.

Level of TBI. Many TBI cases had more than one coding for head injury. Therefore when choosing which type of TBI to use in analysis, a hierarchy had to be formed. It was decided to use concussion, followed by head fracture, intracranial injury, and lastly intracranial injury with hemorrhage, with concussion as the lowest level of TBI and intracranial with hemorrhage as the highest. Head injuries were distributed with 27.3% concussion, 9.1% head fracture, 40.1% intracranial and 23.5% intracranial with hemorrhage. Female and male patients did not vary in terms of TBI level ($p = .14$, $\chi^2 = 5.6$). Increased age was not related to the level of TBI sustained ($F = 1.17$, $p = .32$). Level of TBI was not related to a higher risk of post-TBI depression ($\chi^2 = 1.76$, $p = .62$) or post-TBI CP ($\chi^2 = 5.7$, $p = .13$).

Rates of psychological disorders. Cases of psychological disorders, chronic pain, drug/alcohol abuse, dementia and non-traumatic brain injury post-TBI were identified for the fiscal year following case-finding period (See Table 1). Table 1 also includes ICD-9 codes used and a list of appendices where the drug DINs used are included.

Relationship between Pharmacy and ICD-9 Diagnosis

It will be very important to validate the pharmacy criteria created here through external measures. As a starting point, two-tailed Pearson's correlations were run between cases of anxiety or depression found through ICD-9 coding and those found through pharmacy data. Depression cases found through either method correlated significantly ($p = .01$, Pearsons $r = .38$) as did anxiety cases ($p = .01$, Pearsons $r = .15$). While this does lend some support to our measures, recall that the purpose of using pharmacy data in addition to ICD-9 codings is to find cases that may have otherwise been missed.

Table 1: Rates of various disorders within one fiscal year post-TBI and criteria used.

Disorder	ICD-9 codes	Pharm DIN n(%)	Pre-TBI cases n(%)	Post-TBI cases n(%)
Anxiety	300	See Appendix A	92 (14%)	92 (14%)
Insomnia	None	See Appendix B	177 (27%)	161 (24.7%)
Depression	311, 296	See Appendix C	114 (17.5%)	139 (21.4%)
Chronic Pain	None on its own, see Appendix D	See Appendix D	143 (22%)	42 (6.4%)
Drug and/or Alcohol abuse	303-305,291	None	26 (4%)	68 (10.4%)
Non-traumatic brain injury	310, 434, 438, 436	None	85 (13%)	NA
Dementia	331, 294, 290, 797	None	69 (10.5%)	144 (22.1%)

Survival Analyses

It was hypothesized that cases with pre-TBI CP would show shorter survival times than cases without pre-TBI CP (hypothesis 1). Overall survival curves will be followed by comparisons excluding cancer pain, and comparisons including gender. Lastly medication use is discussed.

Cox Proportional Hazard survival analyses and Kaplan–Meier analyses were undertaken for all-cause mortality. One assumption of Cox survival analyses is that those entering at later time points (e.g. TBI towards the end of the data collection period) do not behave differently than those who entered the data at earlier time points. As the outcomes are independent of the time of injury, this assumption is met.

Cases were traced from the date of their TBI to their last contact point within any one of the current databases. While hospital data includes death at exit, this study does not have access to the Death Registry prior to 1997 for cases at this point. When necessary, probable death was ascertained as described below. Survival analyses include known deaths coded in the hospital data and probable deaths.

Each case was examined and probable deaths were confirmed likely by a physician. Criteria were set to be extremely conservative and thus likely underestimate rate of deaths. Death was conservatively determined probable if: 1) case sustained critical illness (e.g. brain cancer, pneumonia, complications of medical therapy, lung cancer) and then disappeared from all databases (hospital, medical, and pharmacy); 2) ICD death codes were used e.g. (e.g. 797-799). The maximum time until death or censor was 176 months. The last date a case could be traced to in any database for all extant cases was determined, and data were considered right censored beyond that point, meaning that their time of death was judged to be beyond their follow up

period. Possible reasons for censoring include death and moving out of the health areas covered by the databases.

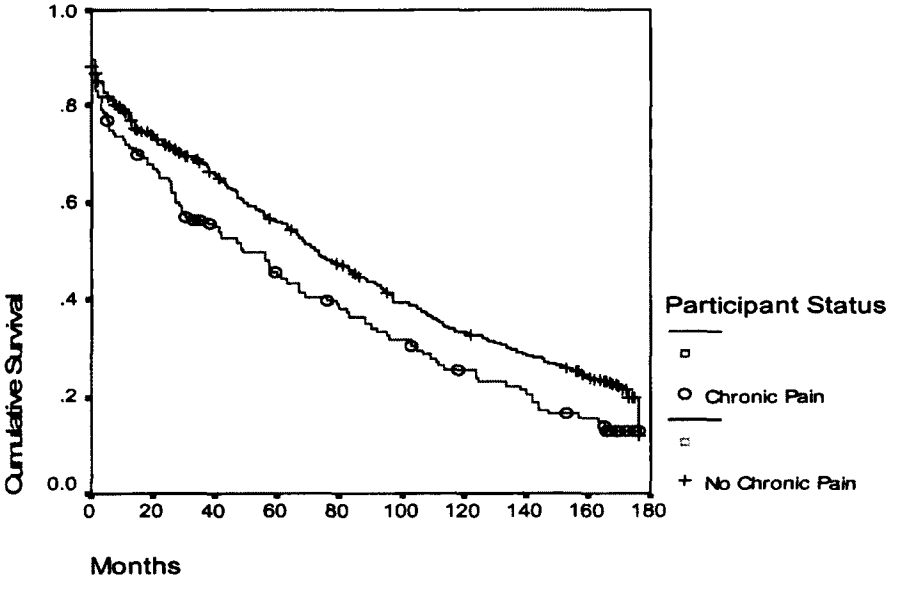
The starting time for all cases was the date of their TBIs. Cases identified as having died in hospital had that date used as their death date. Those identified as very likely dead, using conservative criteria, had their last date in the database in either the pharmacy, hospital, or general billings data used as date of death. Cases not identified as dead had their last date in the database used as a censored date. As death was used as the endpoint, there was only one event to predict. Time between TBI and death or censored date was counted in months. One issue with the longitudinal study of the elderly is that, as the length of follow-up increases, the number of persons at risk at later time points becomes much smaller. A large sample size helps with this issue. There was no significant difference in survival time between male and female cases overall ($p > .05$).

In this study there were 143 cases of pre-TBI CP (22%), and 42 cases of post-TBI CP (6.4%). The two groups did not differ in gender ($p = .4$, $\chi^2 = .5$), age ($F = .06$, $p = .80$), or TBI level. As a reminder, female and male patients did not vary in terms of TBI level ($p = .14$, $\chi^2 = 5.6$) or age ($\chi^2 = .02$, $p = .89$), and increased age was not related to the level of TBI sustained ($F = 1.17$, $p = .32$). In this analysis KM survival curves were used, with survival time in months being the dependent variable, and the presence of CP pre-TBI being the independent variable. It was hypothesized that in cases with CP the survival time would be shorter than in than cases without CP prior to TBI.

Those with CP prior to TBI were found to have a shorter all cause survival time post-TBI than those without prior CP in both KM and Cox survival analyses ($p < .01$, See Figure 2). The KM survivorship curve is included here as well, as it makes use of the data of those dying before

month one of survival, which cases are not used in SPSS Cox survival analyses. In the KM analyses those without CP lived, on average, 15 months longer than those with CP. When the median survival time was used, this difference in survival increased to 24 months. The curve seen here matches a type III survivorship curve where there is a steeper slope for both the CP and non-CP TBI groups directly after TBI, with the non-CP group having a steep decline up to about six to ten months before starting to flatten out, while the CP group continues to have a steep decline until about 30 months post-TBI (Lee, 1980; see Figure 4).

Cox regression survival analyses also showed a significant difference in survival between no pre-TBI CP and those with pre-TBI CP (χ^2 = 8.5, p<.05, C.I. = 1.13-1.764). The risk of death for those with pre-TBI CP is about 1.4 compared to those who did not have pre-TBI CP.



**Note:* P<.01

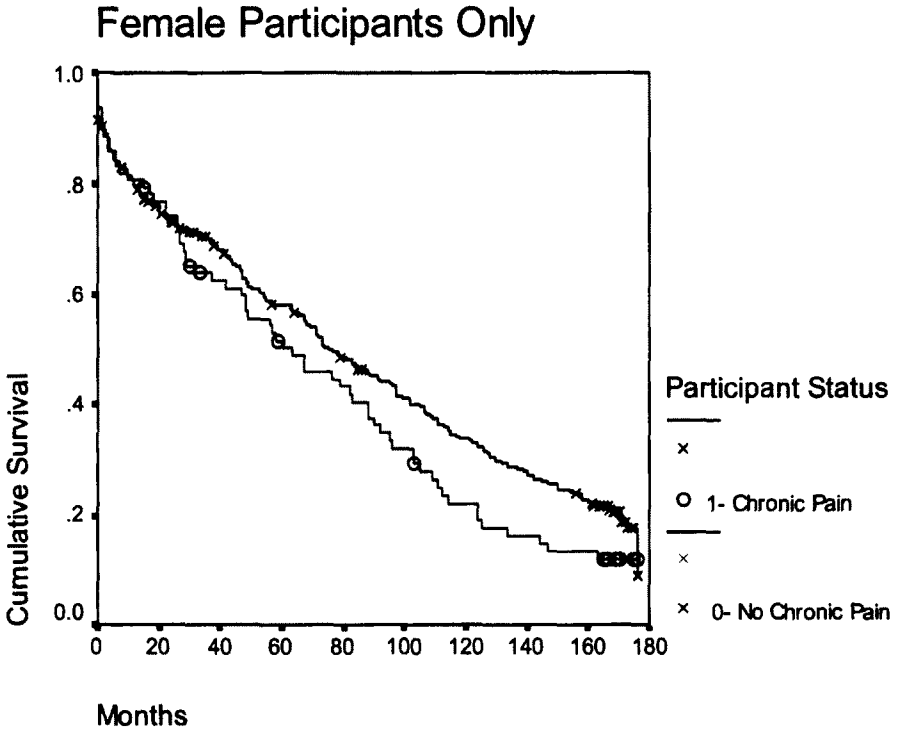
Figure 4. All cause Kaplan-Meier survivorship curves of seniors with and without chronic pain prior to TBI, 1994-2007.

Investigating the effects of cancer pain. One concern was that high levels of pain could be related to cancer, which might then lead to differences in survival times. A comparison was therefore undertaken between cases with and without pre-TBI CP. 13 pre-TBI cancer codes were found in the CP group (9.7%) and 38 in the non-CP group (7.5%). Cases of pre-TBI cancer were removed only from CP group (leaving them in the non-CP group), and the survival curves were rerun. Even in this conservative check, the CP group showed a shorter KM survival post-TBI than the non-CP group ($p = .02$). Cox survival analyses confirmed that those with pre-TBI CP were at increased risk of death even when cancer pain was removed from the CP group ($\chi^2 = 7.76$, $p < .05$, C.I. = 1.01-1.33). The risk of death for those with pre-TBI CP is about 1.2 those who did not have pre-TBI CP.

Investigating the effects of gender. A Cox survival analysis was undertaken whereby gender was entered in the first block before pre-TBI CP. This explanatory variable was not significant ($p = .25$), while pre-TBI CP remained a significant predictor ($\chi^2 = 7.59$, $p < .05$, O.R = 1.18).

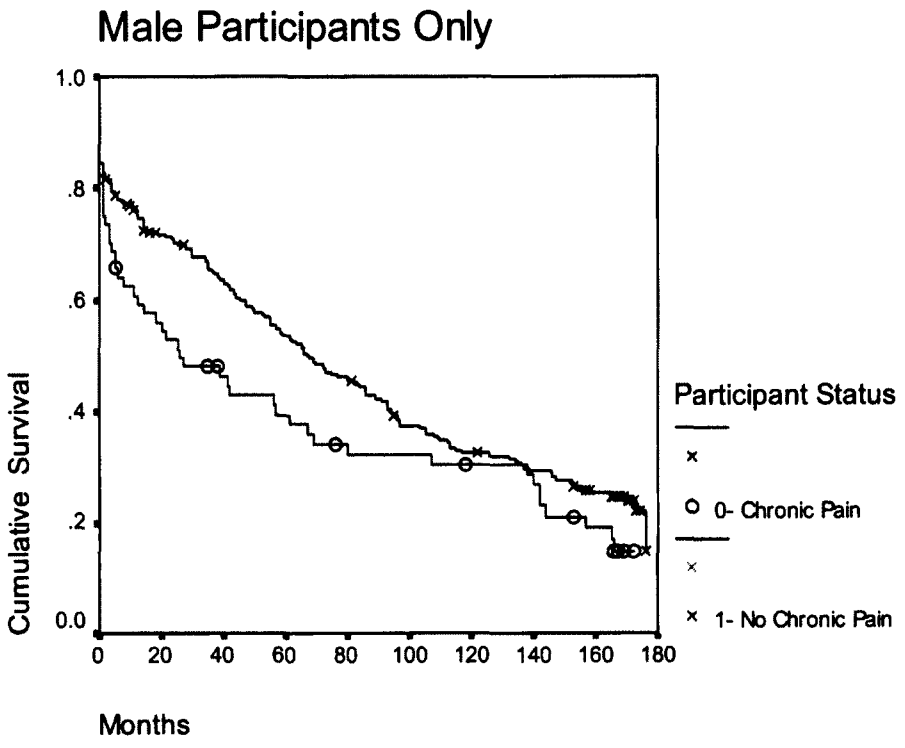
A strength of KM analysis is that it allows the use of very short time intervals (Bewick, Cheeck & Ball, 2004). When KM survival analyses were undertaken separately for male and female cases, CP was a significant predictor of shorter survival for men ($p < .05$), with men with pre-TBI CP living on average 18 months less than men without pre-TBI CP. There was a trend towards shorter survival time in women with CP prior to TBI ($p = .09$). Given the smaller sample size (m = 65, f = 78) it is likely that, with a larger group, both curves would have reached significance. A look at the survival curves highlights another possible reason for this difference. Females with CP showed similar death rates to those without CP at the start of the curve, and the curves slowly separated as those with CP later showed higher death rates and a steeper slope (see

Figure 5). However, in males with CP the slope was substantially steeper very early in the curve (see Figure 6). Recall that chi-square check confirmed that males and females did not differ in the level of TBI they received ($p = .14$, $\chi^2 = 5.6$).



Note: p=.09

Figure 5. All cause Kaplan-Meier survivorship curves comparing female seniors with and without chronic pain prior to traumatic brain injury, 1994-2007.



Note: p<.05

Figure 6. Kaplan-Meier survivorship curves comparing male seniors with and without chronic pain prior to traumatic brain injury, 1994-2007.

Investigating the effects of ICD-9 codes and/or pain medication use on survival. To meet the standards for CP in this study, a case had to meet two sets of requirements. While the criteria for pain severity could only be met using Pharmacare data (high levels of painkillers), long term pain could be assessed either through the long term use of pain killers, or long term use of musculoskeletal ICD-9 codes. A comparison was done between those who had only Pharmacare billings and those whose criteria were made up of both Pharmacare and ICD-9 billings. There was no difference in KM survival curves between these two groups. This, however, does not completely rule out drug effects. Recall that Leipzig et al. (1999) concluded that it was the comorbidity rather than the medications that explained the increased risk of falls/TBI, lending further support to these analyses.

Risk of Depression post-TBI

It was hypothesized that there would be a greater than expected number of depression cases within one fiscal year post-TBI in our cases compared to controls (hypothesis 2), and that this relationship would also be found in cases with milder forms of TBI (hypothesis 2a). Chi-square analyses were undertaken comparing the rates of overall depression, as well the rates of new cases of depression. Lastly, the analyses were repeated using only cases with mild to moderate TBI. Pre-TBI depression was found in 114 cases (17.5%), and 139 cases of depression were found post-TBI (21.4%). The number of findings of depression post-TBI in the cases was compared with the control group of seniors with no prior TBI in the same time period.

Comparison of overall rates of depression. Using a Chi-square analysis, standardized residuals indicate unusually high post-depression levels in those with TBI (6.2) and low levels in control group ($\chi^2 = 50.7$, $p<.001$). The odds ratio was 1.25 (C.I.: 1.2-1.4) indicating that the odds of someone developing depression post-TBI vs. not post-TBI are 1.25:1.

Comparison of risk of new post-TBI cases of depression. The same analysis was undertaken, excluding those who had depression prior to TBI (in the case group) or before the cut-off date (in the control group), to look specifically at new cases of depression within one fiscal year post-TBI. This left 537 participants, 73 being new cases of post-TBI depression. The incidence rate of post-TBI depression in this sample was calculated at 12,739 per 100,000. Once again there was a higher than expected number of cases of depression post-TBI in the cases vs. controls ($\chi^2 = 43.6$, $p<.001$, O.R.= 1.25, C.I. = 1.14-1.37). Contrary to hypotheses, those with pre-TBI CP were not at higher risk of developing new cases of depression post-TBI ($\chi^2 = 2.4$, $p=.15$, O.R. C.I = .884-2.78).

Comparisons using mild to moderate TBI only. Work with seniors has suggested that although TBI represents an increased risk of depression, most work has involved more severe forms of TBI (Raporport & Feinstein, 2001). It was hypothesized that cases with milder forms of TBI would still be associated with an increased risk of depression compared to controls (hypothesis 2b). Chi-square analyses were used to compare the rate of depression within one fiscal year post-TBI in cases with milder forms of TBI (concussion and skull fracture, n = 237) to the rate of depression among controls during the same time period. The same was undertaken for new cases of depression within one fiscal year post-TBI.

There was a significant difference in total instances of depression post-TBI between cases and controls (χ^2= 26.31, p<.0009). Analysis of standardized residuals indicated a higher than expected number of cases in those with post-TBI depression (O.R. = 1.08, C.I. 1.04- 1.1.3).

When investigating new instances of post-TBI depression specifically, there was also a significant difference when comparing cases and controls (χ^2= 23.86, p<.009). 194 cases and 2901 controls were compared. Analysis of standardized residuals indicated a higher than expected number of cases with new cases of depression post-TBI compared to controls (O.R. = 1.11, C.I. = 1.04-1.12).

Risk factors Associated with post-TBI Depression

What psychological and demographic factors are associated with the risk of post-TBI depression in cases (research question 1)? A series of logistic regressions was undertaken to investigate the risk of depression post-TBI in the case group: 1) What factors, including the pre-TBI depression measures, predict post-TBI depression? This was undertaken to explore the relationship between post-TBI depression and other psychological risk factors. 2) What factors, excluding the pre-TBI depression measures, predict post-TBI depression? and, 3) What factors

predict new cases of depression post-TBI? Codings used include female/male (0, 1) and with or without disorder (0, 1).

Variables used in these analyses included pre-TBI depression (except analysis 2), anxiety, insomnia, CP, non-traumatic brain injury (e.g. occlusion of cerebral arteries), dementia, gender, and age. Drug/alcohol use was explored but this variable was omitted, because of the small sample size resulting in low power. There were significant two-tailed Spearman's Rho correlations between some of the psychological variables (See Table 2).

Table 2: Spearman's Rho correlations of select pre-TBI variables.

Variable	Depression	Insomnia	Chronic Pain	Dementia	Non-Traumatic Brain Injury	Gender
Anxiety	.361**	.214**	.143**	.047	.021	-.057
Depression	-	.280**	.137**	.088*	.092*	-.009
Insomnia		-	.244**	.047	.073	-.086*
Chronic Pain			-	-.001	.026	-.023
Dementia				-	.143**	-.043
Non-Traumatic Brain Injury					-	.081*

Note: *= <.05, **= <.01

Predicting post-TBI depression using all variables. What variables predict post-TBI depression within one fiscal year in the cases? In the first forced entry model including all variables, only depression ($p<.001$) and sex ($p<.001$) were significant. To investigate whether important relationships may be masked by a suppressor effect, a backwards regression was also undertaken, which had the same results. The resultant difference in Nagelkerke pseudo- R^2 was .01 or 1%. The overall prediction rate improved very slightly (.2%).

Backwards logistic regressions were undertaken both with and without outliers. The results in both cases were the same. In the final model, gender and pre-TBI depression predicted post-TBI depression (See Table 3). An interaction term was found to be non-significant ($p>.05$). The model correctly predicted 84% of cases. While the model correctly predicted 95.3% of cases without depression, it predicted only 34% of cases with post-TBI depression. This is an improvement over a constant-only model that correctly predicted 81.6% of cases (100% of cases without depression, 0% of cases with depression). Nagelkerke pseudo-R^2 was .36, meaning that roughly 36% of the variation in who had depression post-TBI was accounted for by the model.

Table 3: Logistic regression predicting post-TBI depression with all variables, final model, n=651.

Variable	β	S.E.	Odds Ratio (Exp(B))	C.I.
Gender	1.60	.285	4.94	2.82-8.64
Pre-TBI Depression	-2.82	.271	.059	.035-.101

Note: $p<.000$

Chi Square analysis using standardized residuals confirmed that females were more likely to have depression post-TBI than males ($\chi^2 = 8.58$, $p<.01$, O.R. = 1.77., C.I. = 1.21-2.61) and that those with depression pre-TBI were more likely to have depression post-TBI ($\chi^2 = 109.9$, $p<.01$, O.R. = 1.74, C.I. = 1.47-2.02). Higher-level interactions of these two variables were not significant ($p>.05$).

Predicting post-TBI depression without using pre-TBI depression. It was also of interest to examine which variables aside from pre-TBI depression would predict post-TBI depression, to investigate the relationship between post-TBI depression and other psychological variables that may have been obscured by the strong relationship of pre-TBI depression. To this end, a logistic regression was completed with the assumption that pre-TBI depression was unknown. The procedure was the same as above, however pre-TBI depression was not entered into the analysis.

In the first forced entry model, anxiety ($p = .008$), insomnia ($p = .01$) and sex ($p<.01$) were significant predictors of post-TBI depression. When a backwards regression was undertaken to check for suppressor effects in any of the other variables, anxiety, insomnia and depression remained significant. In the more parsimonious model, the percentage classified correctly remained constant, while change in Nagelkerke pseudo R^2 was also negligible.

In the final model, pre-TBI anxiety, insomnia, and gender combined to predict post-TBI depression (see Table 4). Chi-square analysis using standardized residuals confirmed a higher than expected number of cases with pre-TBI insomnia found in post-TBI depression, meaning those with post-TBI depression were more likely to have pre-TBI insomnia than those without pre-TBI depression ($\chi^2 = 15.32$, $p<.001$), O.R. = 1.28, C.I. = 1.11- 1.48) and a higher than expected number of cases of pre-TBI anxiety in those with post-TBI depression ($\chi^2 = 13.45$,

$p<.001$, O.R. = 1.16, C.I. = 1.05-1.28). As well there was a higher than expected number of females with depression post-TBI compared to males, although the standardized residual was only -1.9 ($\chi^2 = 8.68$, $p<.003$, O.R. = 1.16, C.I. = 1.1- 1.3). The model predicted 80.2% of cases correctly (96.3 % of non-depressed and 7.1% of depressed). Therefore the prediction rates were lopsided. However, this model was able to correctly identify more cases of depression than a constant-only model which identified 0% of cases of depression. Nagelkerke pseudo-R^2 is .181 meaning that roughly 18 % of the variation in who had depression post-TBI was accounted for by the model. A larger sample may help with power in future analyses.

When interaction terms were added into the analysis, gender was no longer a predictor of post-TBI depression, and there was a significant interaction between anxiety and insomnia in predicting post-TBI depression rates (see Table 5). When there are interactions, interpretation of main effects is likely to be misleading. However, this model predicted fewer cases of depression post-TBI (78.5%) and was even more lopsided (0% of depression identified, 100% of non-depressions identified). The Nagelkerke pseudo-R^2 is .082 meaning it only accounted for 8.2% of the variation in cases of depression post-TBI. Therefore for the purposes of this study the regression seen in Table 4 will be used as the final model.

Table 4: Logistic regression predicting post-TBI depression not using pre-TBI depression, model 1, without interactions, n=651

Variable	β	S.E.	Odds Ratio (Exp(B))	C.I.
Insomnia	-1.00*	.23	.37	.23-.57
Anxiety	.98*	.27	2.67	1.58-4.53
Gender	1.32*	.26	3.74	2.27-6.12

Note: * p <.001*

Table 5: Logistic regression predicting post-TBI depression not using pre-TBI depression, model 2, with interactions, n=651

Variable	β	S.E.	Odds Ratio (Exp(B))	C.I.
Insomnia	-.92*	.212	.40	.266-.610
Anxiety	.476*	.20	1.61	1.08-2.39
Anxiety by Insomnia	1.32*	.34	3.68	1.90-7.13

Note: * p<.001

Predicting new cases of depression post-TBI. For the final analysis all cases with pre-TBI depression were excluded. After the exclusion of those with pre-TBI depression and outliers, 513 cases remained. In the first forced model entry, including all variables with the exception of pre-TBI depression, the only predictor variable to reach significance was sex (p = .003). A backwards logistic regression was then undertaken to attempt to uncover any further

relationships masked by having all the variables in the model. The backwards regression suggested that pre-TBI non-traumatic brain injury may be worth considering. The change in Nagelkerke pseudo-R^2 associated with fewer variables was negligible (.002). The prediction rates between the full model and the more parsimonious model were equal both in those with and without new cases of depression post-TBI.

In the final model, gender and previous non-traumatic brain injury (e.g. occlusion of cerebral arteries) were predictive of new cases depression (see Table 5). The relationship between new cases of depression and non-traumatic brain injury was not strong, with the upper end of the O.R. confidence interval approaching one (.98). Part of this may be due to the low number of cases in the dataset (n = 59). The O.R. would need to be interpreted with extreme caution due to the coefficient flipping in this data. Chi-square analyses using standardized residuals confirmed that there was a trend towards more cases of previous non-traumatic brain damage in those experiencing post-TBI depression ($\chi^2 = 3.01$, p = .083, O.R. = 1.09. C.I. = .97-1.21). What is interesting is that non-traumatic brain injury was a stronger predictor of new cases of post-TBI depression than psychological variables such as anxiety and insomnia. Chi-square analyses using standardized residuals confirmed that there were fewer cases of depression post-TBI in males than females ($\chi^2 = 8.07$, $p<.005$, O.R. = .78, C.I. = .67-.91). An interaction term was added and found to be non-significant ($p>.05$).

This model correctly predicted 89.5% of cases. However, while it predicted 100% of cases without depression, it was unable to predict cases with depression with any accuracy, and the rate of correct prediction was not improved by the model. Nagelkerke pseudo-R^2 was .04 meaning that roughly 4% of the variation in who developed depression post-TBI was accounted for by the model. A larger sample may help with power in future analyses.

Table 6: Logistic regression predicting new case of depression post TBI, final model, n=513.

Variables	B	S.E.	Odds Ratio	C.I.	
				Lower	Upper
Non-traumatic brain injury	-1.449**	.40	.24	.11	.51
Gender	2.531**	.49	12.56	4.78	33.05

Note: p<.001

Characteristics of Pre-TBI CP

Is there a profile of characteristics that distinguishes seniors with CP prior to TBI from those without? It was hypothesized that those with prior CP would show a higher level of prior co-morbidities such as depression, anxiety, and insomnia (hypothesis 3).

Since the dataset contained many categorical variables with more than two categories and the group variable is dichotomous (prior CP vs. no prior CP), it was preferable to use a backwards discriminative modeling approach in logistic regression rather than collapsing predictor variables into dummy variables. As well, the data failed to meet many of the requirements necessary for discriminant function analysis. Therefore logistic regression is preferable as it makes fewer assumptions about the variables and with a large sample size, the difference between discriminant modeling and logistic discriminant analysis is small (Pohar, Blas & Turk, 2004). Can group membership be reliably predicted from the set of variables available? What are the patterns of differences between these two groups?

Variables used included pre-TBI psychological disorders (anxiety, insomnia, and depression), dementia, non-traumatic brain injury, age at time of injury, and gender. In an entry

model where all variables were forced in on the first step, insomnia ($p<.001$) and anxiety ($p<.04$) were significant predictors of pre-TBI chronic pain. Because many of the variables are related to each other and important relationships may be masked, a backwards regression was undertaken as well to determine the importance of the variables. The combined variables removed lowered the Nagelkerke R-square by .004, far less than a 10% change in significance.

Once again a backwards model was used due to the correlations between some of the variables. There were no outliers in this analysis. In the final model both anxiety and insomnia predicted group membership (Table 6). Those with CP had nearly twice the odds of also having an anxiety disorder (1.89). Chi-square analysis with standardized residuals confirmed the presence of more than the expected number of anxiety cases in those with pre-TBI CP ($\chi^2 = 14.05$, $p<.0001$). A confirmatory chi-square using standardized residuals confirmed the hypothesis that there would be a higher than expected level of insomnia in cases with pre-TBI CP ($\chi^2 = 41.07$, $p = .083$, OR = 1.38, C.I. = 1.22-1.57), as well as anxiety ($\chi^2 = 14.04$, $p<.001$. O.R. = 1.16, C.I. = 1.1-1.3). Recall that the Spearman's correlation between anxiety and insomnia was significant (.214) and multicollinearity may have a suppression effect, meaning that the relationships found here are very conservative estimates.

This model predicted 78.4% of group membership correctly (95.6% of those without CP, 16.9% of those with CP). Therefore, the prediction success rate was lopsided. However, this model was less lopsided than a constant-only model which predicted 100% of those without pre-TBI CP and 0% of those with pre-TBI CP. Each step in the backwards logistic regression resulted in an increased correct percentage of patients with pre-TBI CP identified. The full model showed only a .3% increase in group prediction accuracy. Nagelkerke Pseudo- $R^2 = .103$.

Therefore, although the model is significant, it accounts for only 10.3% of the variability in pre-TBI CP. A larger sample size may shed further light on these relationships.

Table 7: Logistic regression predicting group membership of pre-TBI chronic pain cases, final model n =651.

Variables	B	Wald	S.E.	Odds Ratio	C.I.	
					Lower	Upper
Insomnia	-1.16**	31.92	.21	.314	.21	.47
Anxiety	.98*	13.3	.26	2.6	1.15	3.1

Note: **p<.001 * p<.02

Predicting post-TBI Chronic Pain

Can pre-TBI variables be used to predict which seniors will develop new cases of CP within one fiscal year post-TBI (research question 2). To look at this issue, a logistic regression was undertaken including anxiety, insomnia, depression, dementia, non-traumatic brain damage, age at injury, and gender. Chi-square analysis confirmed that TBI severity was not related to post-TBI CP (trend towards more cases of previous non-traumatic brain damage in those experiencing post-TBI depression ($\chi^2 = 3.01$, p = .067, O.R. = 1.1. (C.I. = .97-1.25).

In a forced entry model, no variables were significantly related to post-TBI CP. In the final backwards model no variables (excepting constant) were significant. The variable closest to achieving significance was age (p=.09). The model accounted for 1.1% of the variability in CP

post-TBI and did not result in any change in correct group predictions. As the sample size was very limited (n = 42 or 6.5% of cases), lack of power is a serious issue in this analysis and it should be considered only exploratory.

IV. Discussion

Using data from three different sources to identify cases, the results of this study have been able to demonstrate a significantly shorter survival period for those with CP prior to TBI than those without. TBI in the elderly has also been demonstrated to be a risk factor for the development of depression, even in cases of milder TBI.

Chronic Pain

Pre-TBI CP is related to shorter survival times. As hypothesized, pre-TBI CP was associated with shorter survival times than those without CP (hypothesis 1). The risk of death for those with pre-TBI CP was 1.4 compared to those who did not have pre-TBI CP. Not all studies have found this difference in survival times in older populations. Andersson (2009) found no difference in survival between seniors with and without CP. However, in their study, only those in the youngest senior age group were included (ages 65-79) and made up a relatively small portion of their study, limiting power. Jacobs, Hammerman-Rozenberg and Stessman, 2005, found that low back pain was not a predictor of early death in women, and paradoxically seemed to have a protective effect in men. The authors later concluded that an interaction between pain and number of doctor's visits explained a significant part of this relationship, suggesting that males with low back pain were more likely to go see a doctor, and therefore receive early or preventative health care. Therefore the current study adds to the literature by showing that the relationship between pain and shorter survival times (post-TBI) does hold true in an elder

population. Future analyses should include the control group to address survival time in a non-TBI elder population.

Some have suggested that differences in mortality rates between those with and without CP may result from deaths due to cancer (Jordan & Croft, 2010). In an extremely conservative test where cancer cases were removed from the CP but not from the non-CP group, the results of this study remained significant. Therefore the differences in death rates in this study are likely due to non-cancer factors.

Several hypotheses have been proposed for this difference in survival. Andersson (2009) conducted a survival study, over twenty years, of persons with widespread pain, and found differences in survival time between CP and non-CP groups which were significant when age and sex were controlled for. These significant differences disappeared when specific lifestyle factors were taken into account. In their final model, low physical activity level and smoking, both of which have been found to be related to CP, accounted for the difference in survival time between the two groups. A longitudinal study would be required to determine whether the lifestyle changes came before or after the CP. The authors noted that 'These factors could be regarded as downstream variables that are in turn due to upstream variables such as socioeconomic status, culture and education" (p. 1985). One important implication of this result is that the treatment of CP should take care to involve lifestyle factors such as exercise and quit smoking programs. In explaining the shorter survival time in those with severe CP in their study, Torrance et al. (2010) suggested that the intensity of the pain, as well as the disability associated with the high levels of pain were related to the shorter survival times, rather than the cause of the pain itself. Andersson (2009) suggested that cognitive-behavioural methods commonly used in CP programs could well be used in addressing lifestyle factors. In support of this, Turner (in

press) has recently published a commentary on the growing support for the use of cognitive-behavioural therapy (CBT) in seniors with chronic pain. Research would first need to demonstrate the effect of lifestyle factors on longevity in a senior population, with or without TBI which may be difficult "... due to shorter time of exposure of negative lifestyle factors associated with CP" (Andersson, 2009, p. 1986). A study showing the effect of CBT in addressing these issues in an elderly CP population would be a useful next step.

Other proposed causes have included increased stress (and long term exposure to cortisol; Andersson, 2009; Torrance et al., 2010). Chronic pain has been linked to elevated cortisol levels, as well as abnormal endocrine responses to stress, which may explain the increased risk of cardiovascular related death seen in those with CP (Torrance et al., 2010).

Jansson, Mittendorfer-Rutz and Alexandersson (2012) conducted a large cohort study of survival of those with musculoskeletal disorders. The authors used Swedish registers to compare survival times for those with work-related absences for musculoskeletal reasons, for other reasons, or those who lacked sick days over a three year period. While those with work absences for any reason did show shorter survival times than those without work absences, the most interesting results were obtained when those with musculoskeletal vs. non-musculoskeletal absences were compared. Those with musculoskeletal issues showed increased mortality risks for death due to mental disorders (ICD-10, F00-F99) and suicides, after controlling for socio-demographic factors and morbidity. This suggests that psychological factors have a larger role in early death in those with sickness absences due to musculoskeletal reasons vs. those with sickness absences due to all other reasons. The authors suggest this is due to the high levels of psychological comorbidities often seen in CP populations, as well as an increased risk of psychological comorbidities such as depression due to sickness absences. However this study

was not limited to an elder population. One important follow-up to the current research would be to look at the cause of death through death codes, particularly when more in-depth death data becomes available. While work-related absences may not pertain to increased risk of psychological disorders in an elder population, Jansson et al. (2012) suggest the increased risk may also be created through increased social isolation, decreased activity, and sleep issues associated with pain. If the higher rate of deaths due to psychological disorders and suicide holds true in an elder Canadian population, the implications are that health workers should be more effectively screening/treating mental disorders in this group, as well as increasing vigilance about suicide risk.

There was no significant difference in survival CP cases identified using both ICD-9 codes and ICD-9 codes in conjunction with drug DIN. There was a possible gender difference, with the survival curves being significantly different in men, while there was a trend towards shorter survival time in women. With a large sample size lending more power, the difference would likely be significant for both groups. Visual inspection of the survival curves indicates a steeper mortality rate for males than for females with CP in the initial post-TBI period.

Characteristics of pre-TBI CP. As hypothesized, cases with pre-TBI CP were separated from non-CP cases by psychological factors: anxiety and insomnia (hypothesis 2). This is an important finding and it is hypothesized that these variables are often interrelated, feeding off of each other. For example, pain may lead to higher rates of insomnia, which may then increase the pain further. Future studies could examine these relationships in an elderly population. For example, does age-appropriate treatment of anxiety or insomnia in the elderly result in lower levels of pain?

Predicting post-TBI CP. Logistic regression failed to identify any variables that could predict development of CP post-TBI (research question 2). This may be due in part to the low number of cases of depression post-TBI (6.4%) which would result in a lower power. Future research could address this question from a longitudinal standpoint, including more lifestyle issues such as activity levels, social isolation, etc.

The rate of CP found one year post-TBI was lower than expected (6.4%). To meet the criteria for CP a participant would have had to be in pain for over 3 months. This means that those who did not survive past the 3 month period could not have been considered for this group, which may account for the lower prevalence compared to studies that allowed for a diagnosis of CP using pre and post-TBI measures combined.

Depression

TBI is related to an increased risk of depression. As hypothesized, cases were at higher risk of post-TBI depression than controls (hypothesis 2). Cases were also at a higher risk of developing depression post-TBI than a control group of seniors without TBI. Analyses confirmed that the higher levels of depression found post-TBI remained significant when only mild to moderate TBI was examined (hypothesis 2b). Recall that cases came from both ICD-9 codings and pharmacy data. A wide range of antidepressants were used, with those related to a higher risk of falls being a subset of them (see Appendix C).

Risk factors related to post-TBI depression. Factors predicting post-TBI depressions were investigated (research question 1). The strongest predictors of post-TBI depression included gender and pre-TBI depression. This fits with prior research by Bombardier et al. (2010) where pre-TBI depression was also found to be a risk factor for post-TBI depression. While research

has examined the effect of TBI on depression risk, less research has been done using an elderly population, and it has largely focused on more severe forms of TBI.

When pre-TBI depression was not entered into the equation, gender, anxiety and insomnia were all significant predictors of post-TBI depression, suggesting that these may be important variables to screen for when assessing depression risk shortly post-TBI.

Risk factors related to the development of new cases of depression post-TBI. Investigations predicting new cases of post-TBI depression found that gender and pre-TBI non-traumatic brain injury were significant predictors of post-TBI depression. However the relationship between pre-TBI non-traumatic brain injury and post-TBI depression was small (OR= .24), and confirmatory chi-square analyses used was unable to detect a significant relationship. The fact that female participants were at higher risk of post-TBI depression in all analyses suggests that special vigilance in screening this population is necessary.

When interpreting the logistic regressions undertaken, it is important to keep in mind that many of the variables were found to be correlated with each other. This means that in a regression they will likely have a suppressor effect on each other, and any relationships found will likely be underestimated. When looking at the βeta weights, it is important to keep in mind that in a multiple regression it is impossible to interpret each βeta weight separately as they are dependent on the other variables in the model.

Rates of depression. The rates of depressive disorders found in this study fit with the expected rates for a senior population. For example, approximately 15.8% of Canadian seniors have CP, a rate that is slightly lower than the rate of 22% found in this study (Reitsma, Tranmer, Buchanan, & VanDenKerkhof, 2011).

The rate of post-TBI depression found in this study was 21.4%. This is lower than Pagulayan et al.'s (2008) estimate of up to 30% experiencing post-TBI depression within the first year. However given that patients often go six months before treatment for depression begins, it is not unexpected that determinations based on treatment measures rather than mood questionnaires would lead to an underestimation (Levin et al., 2005). Recall that some antidepressants have been identified for use in early dementia. While there was a significant non-parametric correlation between the depression cases and dementia cases found in this study, the overlap was small (Rho= .088, $p<.05$), suggesting that this was not a large issue in this study. Future research could involve a chart review to identify the reason for the use of antidepressant medications.

Other Disorders

Published literature suggests a 15% rate of anxiety disorders in a senior population (Vink, Aartsen & Schoevers, 2008). The present study found a rate of 14% when using multiple methods to identify cases. Approximately half the cases were identified using pharmacy data. This speaks to the critical need to have more than one marker used for psychological issues when working with administrative databases, in order to avoid underestimating results. Relying solely on medical billings would likely have underestimated the number of anxiety disorders in this population. This would have resulted in less power to find important relationships involving anxiety, such as the relationship between pre-TBI anxiety and the development of post-TBI depression.

The rate of insomnia identified is of special interest, as it was the only variable for which no ICD-9 codes were used. Cases of insomnia were derived from Pharmacare data. The current research resulted in an insomnia rate of 27% pre-TBI. In the Canadian population it has been

estimated that 31% of seniors aged 65-74 have insomnia, while 36% of those aged 75 and up have insomnia (Sutton, Moldofsky & Badley, 2001). The numbers in the current research were therefore slightly conservative, as expected. Sutton, et al. (2001) also found that severe pain was strongly related to insomnia (OR= 1.99). In our data, insomnia and CP were correlated (Nagelkerke pseudo-R squared= .244, p>.005). Both of these findings lend support to the use of Pharmacare data in appropriately identifying insomnia cases.

Frailty

It is hypothesized that many of the variables measured are interrelated in increasing TBI risk, and also the risk of poorer outcomes including shorter post-TBI survival times, and that these fall under the umbrella of frailty (Figure 1). Frailty is a progressive age-related syndrome including factors predisposing seniors to TBI (Chang, Chan, Kuo, Hsuing & Chen, 2010). While there are many definitions of frailty, all include the idea that multiple systems or pathologies are involved (Topinkova, 2008). Frailty involves decreased resistance to stress, lowered reserves (cognitive, physical etc), loss of weight, and balance issues not expected as a result of normal aging-related changes (Cochen et al., 2009; Fried et al., 2001). In discussing the increased risk of death and psychological co-morbidities associated with CP, some researchers have begun to use the model of allostatic load, where exposure to stressors over a lifetime lowers the body's ability to appropriately respond to new stressors (Dominick, Blyth & Nicholas, 2012; Sibille, & McEwman, B, 2012; van der Windt, 2012). When conducting research in an elderly population, both the model of allostatic load and frailty may apply, and are likely related to each other.

Many of the interrelated issues involving TBI risk in the elderly may be rooted in frailty. It is hypothesized that the variables shown in Figure 1 are not only related to TBI in the elderly,

but may also be rooted frailty and interact/feed into each other. As a result, frailty will also increase susceptibility to the effects of TBI (Leblanc et al., 2006).

This study has confirmed that, within this model, many of the TBI risk factors are related to each other, such as depression, anxiety, insomnia, and chronic pain. This allows many possible avenues for treatment. Many of these factors have also been shown to be related to post-TBI outcomes, with depression, anxiety and insomnia related to post-TBI depression.

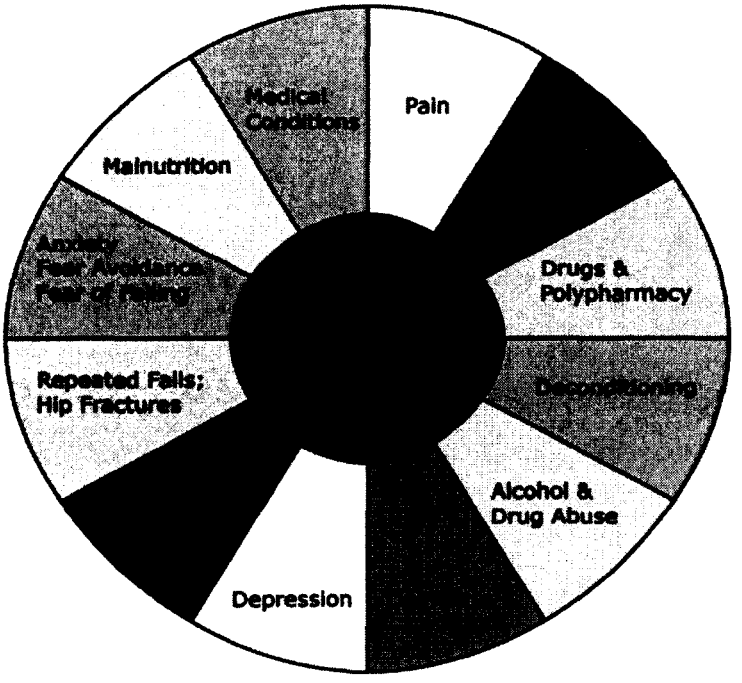


Figure 1: Risk factors associated with traumatic brain injury in seniors

The current study is only a small start in exploring this model. Any risk factor left untreated may accelerate further decline in multiple areas, leaving seniors increasingly vulnerable to falls, TBI, and poorer outcomes post-TBI. Frailty not only has been seen to increase the risk of falls itself, but also to increase the risk of comorbidities seen within this model that act to increase the risk of falls, such as medical disorders like hypertension (Ahmed,

Mandel & Fain, 2007). In recent studies, researchers pinpointed a large dose-dependent relationship between vitamin D deficiencies and both frailty and pre-frailty in the elderly, possibly due to decreased musculoskeletal function (Chang et al., 2010; Topinkova, 2008).

As part of a fall prevention program for seniors in Canada, Fletcher, Guthrie, Berg and Herders (2010) found that the higher the self-reported pain levels, the more a participant was at increased risk of activity restriction related to fear of falling. Recall that Andersson (2009) found that lifestyle issues such as activity levels accounted for the shorter survival times in those with CP. This highlights how pain itself can feed into lower levels of activity, potentially increasing frailty, and risk of poorer outcomes.

Research addressing this model as representing risk factors for TBI and poorer outcomes post-TBI represents a possible line of research. Once important variables in TBI risk and TBI outcome are identified, knowledge translation , defined by the Canadian Institutes of Health Research as "...application of knowledge to improve the health of Canadians, provide more effective health services and products, and strengthen the health care system" will become important (CIHR, 2013). It is important to ensure that information is widely disseminated to ensure that both doctors and patients have the information they need to make effective health care decisions.

For example, with a better knowledge of the factors involved in mortality risk in those with pre-TBI CP, studies could be undertaken to investigate which group(s) are at highest risk(s) of these effects, how to screen to identify the groups at highest risk, and possible points of intervention. One could also investigate the usefulness of anxiety, insomnia, and non-traumatic brain injury screens shortly post-TBI in identifying those most at risk of post-TBI depression. Once effective screening tools and increased risk were established, the next step would be to

identify possible interventions to lower post-TBI depression, targeting the high risk groups. Factors that can affect health care decision-making involve knowledge of modifiable risk factors for poor post-TBI outcomes in seniors, and barriers to the assessment/screening of relevant post-TBI psychological variables, as well as barriers and best practices in the recognition and treatment of relevant psychological variables.

Limitations of the Data

While these results are important and help to fill in some important gaps concerning research involving TBI in the elderly, there are a few limitations to this study. Milder TBI cases and/or those who simply did not seek medical attention will have been missed, meaning that all estimates of TBI are likely to be underestimates (Corrigan, Selassie & Orman, 2010). While TBI is often defined by states of consciousness, information in hospital records is often limited to ICD codes, and includes little information on severity of the TBI. Information present concerning the type of TBI (e.g. concussion, intracranial injury) allows for a broad idea of TBI severity.

In epidemiological studies, one is often dependent on information and coding done by another party (Picket et al, 2004). The Canadian Institute for Health Information (CIHI) has strict training and quality control procedures for the coding of medical records, and hospital diagnoses are coded by medical records personnel who have been trained for accuracy (Picket et al., 2004). Consequently one would expect the data used here to be acceptably accurate. However, a chart review to confirm the accuracy of the dataset was not currently available, and would be a good area for further research.

Because some of the cases were defined using Pharmacare data, it may be difficult to tease apart the effects of psychological conditions from the prescriptions used to treat them.

There are issues in whether the risk of fall/head injury is due to medications or the psychological issues themselves, as both are risk factors for fall/head injury (Campbell, Robertson, Gardner, Norton, & Buchner, 1999). It is extremely difficult to tease these issues apart, as they will often co-occur. This issue is ubiquitous in health research.

In a similar vein, it is not always possible to know with absolute certainty why some of the medications were prescribed. Antidepressants may be used for depression, headaches, anxiety, or insomnia, depending on dosing, concurrent prescriptions, etc. Ziere et al. (2006) call this "confounding by indication" (p.222). This was controlled for in the present study by the use of strict conservative rules, made with the help of multiple doctors, taking these differences and uses specific to a senior population into account when using Pharmacare data to identify cases. Every effort was made to err on the side of underestimating rather than overestimating psychological disorder. In support of Pharmacare use, the proportion of participants with anxiety, insomnia, depression and CP fall within the expected range, and there were significant Pearsons correlations found between both anxiety cases found through Pharmacare vs. ICD-9 coding, and between depression cases found through Pharmacare vs. ICD-9 coding. Lastly, the number of cases was smaller among the oldest old, decreasing the power of analyses in this group.

Lastly it is important to understand that this analysis only captures cases who presented for treatment at some point in time. There will be a subset of seniors that do not present for treatment or mention depression or other psychological issues, and these will be missed in this analysis (Butler, Cohen, Lewis, Simmons-Clemmons & Sunderland, 1997). Sambamoorthi, Walkup and Akincigal (2003) noted that the elderly were less likely to receive treatment for their depression than younger populations. In the elderly it is common for depression to be associated with high levels of comorbidity, making awareness and identification of depression in this

population all the more difficult (Charlson & Peterson, 2002). Therefore even with the addition of pharmacy data, any estimates of prevalence of psychological disorders based on administrative data will likely be an underestimate of the true prevalence.

V. Conclusion

This research is unique in its use of multiple databases, and the creation of exacting criteria for depression, CP, insomnia, and anxiety, using pharmacy data over time. The in-depth use of administrative information allows a fresh look at the role that multiple psychological disorders play over time in TBI in seniors. Pharmacare data was successfully used in conjunction with ICD-9 coding in identifying cases of anxiety, insomnia, depression, and chronic pain. The current research demonstrates that it is possible to obtain psychological factors in administrative datasets, and to use data linkage to study important questions concerning public health.

Groundbreaking use of multiple databases and a large follow-up time has unlocked a vast amount of information, which this thesis has only begun to uncover. There are many psychological and other factors involved in TBI risk in seniors and these factors are often interrelated, as illustrated in Figure 1. The model proposed did not include non-traumatic brain injury, which this research suggests is a variable that may be well worth including in future studies. Future research in this area may involve a closer look at these variables, their interconnection, and their relationship to outcomes. Further use of the control group would allow comparisons of rates of psychological disorders well beyond one year post-TBI. Other variables (e.g., diabetes, estrogen use) can be examined and, in fact, have been coded in the dataset for further analysis. The information thus gathered, with a large sample size over many years, will allow a unique and innovative look into the issues of TBI in the elderly.

When using administrative databases, one is limited by the amount of information already gathered (Jacob, 1984). It will be very important in the future to continue to validate the pharmacy measures of psychological disorders created here, through external measures such as chart review, questionnaires, and interviews, etc. When establishing convergent validity, there are several methods discussed by Sullivan and Feldman (1979) that could be employed to establish the validity of these measures. There may be modifications that could be made to the criteria that would increase their sensitivity/specificity.

Palin et al. (2012) conducted a study comparing mental health codes found in British Columbia health datasets to those found in a mental health survey using person-by-person data linkage. This investigation was undertaken when it was found that the prevalence of mental health issues differed substantially between the two methods, with the reports from the survey results showing much lower estimates of mental health issues than reports based on ICD-9 codings from health databases. One of their findings was that seniors (aged over 60) were likely to underreport mental health care in the survey, possibly due to differential recall. This is one issue that will need to be kept in mind when validating the Pharmacare measures through external sources.

Torrance et al. (2010) stressed the need for longitudinal studies examining the relationship between survival time and CP. Smith (2010) suggested four possible reasons for the relationship between CP and shorter survival times: "(1) pain and/or musculoskeletal diseases causes death and/or cancer (2) the same factors that cause pain and/or musculoskeletal disease also cause death and/or cancer (3) other factors and pain/musculoskeletal disease combine to cause death and/or cancer (4) the findings arrive through chance" (p.e112). Without this knowledge, it will be difficult to know how to address this relationship. One fruitful line of

research could be to follow seniors over time, identifying those who developed CP, and looking at survival time while considering covariates such as other medical disorders, psychological disorders, lifestyle factors, etc.

As many of these factors such as depression, anxiety, insomnia and pain are modifiable and currently undertreated, research could uncover issues leading to lower risk of TBI and better outcomes post-TBI in seniors. In the current study, cases with CP showed significantly shorter survival times than those without pre-TBI CP, even in the most conservative analysis. Theories concerning the cause(s) for this difference include lifestyle factors, and other issues.

Studies should examine the effect of treating psychological variables post-TBI on cognitive function, psychological dysfunction, activities of daily living, etc. Unfortunately, all too often, psychological factors are undertreated post-TBI (Bedard et al., 2012). In the present study seniors with mild to moderate forms of TBI were at increased risk of post-TBI depression compared to controls, suggesting that even those with milder forms of TBI and/or no depression in the year previous to the TBI should be considered at risk of post-TBI depression, and screened accordingly. Recent studies have suggested that mindfulness-based cognitive therapy can be effective in lowering depression rates post-TBI, and further research could be conducted specifically in a senior population (Bedard et al., 2012). Further studies are needed to see if this change is maintained, and how it relates to other factors.

In conclusion this study has established the ability to use administrative databases, including pharmacy information when studying psychological variables. Chronic pain prior to TBI in seniors was associated with significantly shorter survival times, even when controlling for cases of cancer. TBI in seniors was a risk factor for the later development of depression in general, and also when only milder forms of TBI were investigated. As hypothesized, pre-TBI

CP was associated with psychological variables such as anxiety and insomnia, while no variables were able to accurately predict risk of post-TBI CP. In investigating risk factors for post-TBI depression, the results varied, depending on whether one considered all depression or limited analysis to new cases of depression. In both cases female gender was an important risk factor. Overall, pre-TBI depression, anxiety and insomnia were risk factors for depression, while pre-TBI non-traumatic brain injury was a risk factor for new cases of depression. This study highlights the important effect psychosocial variables have on the quality and quantity of life post-TBI in an elderly population.

VI. References

Abelson-Mitchell, N. (2008). Epidemiology and prevention of head injuries: Literature review. *Journal of Clinical Nursing, 17*(1), 46-57.

Ahmed, Mandel & Fain (2007). Frailty: An emerging geriatric syndrome. *The American Journal of Medicine, 120*, 748-753.

Amacher, A.L. & Byee, D.E (1987). Toleration of head injury in the elderly. *Neurosurgery, 20*, 954-958.

Andersson, H.I. (2009). Increased mortality among individuals with chronic widespread pain related to lifestyle factors: A prospective population based study. *Disability and Rehabilitation, 31*(24), 1980-1987.

Annagers, J.F., Grabow, J.D., Kurland, L.T. & Laws, E.R. (1980). The incidence, causes, and secular trends of head trauma in Olmstead country Minnesota, 1935-1974. *Neurology, 30*, 912-919.

Bay E, & Donders J. (2008) Risk factors for depressive symptoms after mild-to-moderate traumatic brain injury. *Brain Injury, 22*(3), 233-241.

BC Brain Injury Association (n.d) *Acquired Brain Injury,* http://www.bcbraininjuryassociation.com/acquired.php Accessed February 15, 2010.

Bedard, M., Felteau, M., Marshall, S., Dubois, S. Gibbons, C., Klein, R. & Weaver. B. (2012). Mindfulness-based cognitive therapy: Benefits in reducing depression following a traumatic brain injury. *Advances in Mind Body Medicine, 26*(1), 14-20.

Bewick, V, Cheek, L. & Ball, J.B. (2004). Statistics review 12: Survival analysis. *Critical Care, 8*, 389-394.

Bickel, P.J. , Hammel, E.A. & O'Connell, W.O. (1975). Sex bias in graduate admissons: Data from Berkley. *Science, 187*(4175), 398-404.

Bischoff-Ferrari, H.A., Dawson-Hughes, B, Willwett, W.C., Staehelin, H.B., Bazemore, M.G, Yee, R.Y. & Wong, J.B. (2004). Effect of vitamin D on falls: A meta-analysis. *Journal of the American Medical Association, 291*(16), 1999-2006.

Bischoff, H.A., et al. (2003). Effects of vitamin D and calcium supplementation on falls: A randomized controlled trial. *Journal of Bone Mineral Research, 18*(2), 343-351.

Bewick, V, Cheek, L. & Ball, J.B. (2004). Statistics review 12: Survival analysis. *Critical Care, 8*, 389-394.

Bombardier, C.H., Fann, J.R., Temkin, N.R., Esselman, P.C., Sureyya , S.B. & Dikmen, S. (2010). Rates of Major Depressive Disorder and clinical outcomes following traumatic brain injury, *Journal of the American Medical Association, 309*(19), 1938-1945.

Brennan, N. (n.d.) *The GNU Awk user's guide*. Retrieved from http://www.gnu.org/software/gawk/manual/gawk.html

Bruns, J. & Hauser, W.A. (2003). The epidemiology of traumatic brain injury: A review. *Epilepsia, 44*(10), 2-10.

Butler, R.N., Cohen, G., Lewis, M..I, Simmons-Clemmons, W., & Sunderland, T. (1997). Late-life depression: how to make a difficult diagnosis. *Geriatrics, 52*(3), 41-2, 47-50.

Cairney, J. , Corna, L., Veldhuizen, S., Herrmann, N. & Streine, D.L. (2008). Comorbid depression and anxiety later in life: Patterns of association, subjective well-being, and impairment. *American Journal of Geriatric Psychiatry, 16*(3), 201-208.

Campbell, J., Robertson, C., Gardner, M.M., Norton, R.N. & Buchner, D.M. (1999). Psychotrophic medication withdrawal and a home-based exercise program to prevent falls: A randomized, controlled trial. *Journal of the American Geriatric Society, 47*(7), 850-853.

Chang, C.I., Chan, D.C., Kuo, K.N., Hsuing, C.A. & Chen, C.Y. (2010). Vitamin D insufficiency and frailty syndrome in older adults living in a northern Taiwan community. *Archives of Gerontology and Geriatrics, 50*(1), S17-S21.

Charlson, M. & Peterson, J.C. (2002). Medical comorbidity and late life depression: what is known and what are the unmet needs? *Biological Psychiatry, 52*(3), 226-235.

Canadian Institute for Health Information (CIHI) (2006). *Head Injuries in Canada a Decade of Change.* Retrieved from https://secure.cihi.ca/free_products/ntr_head_injuries_2006_e.pdf

Cochen, V., Arbus C., Soto, M.E., Villars, H., Tiberge, M., Veccherini, M.F., ...Vellas, B. (2009). Sleep disorders and their impacts on healthy, dependent, and frail older adults. *The Journal of Nutrition, Health & Aging, 13*(4), 322-329.

Corrigan, J.D., Selassie, A.W., Orma, J.A. (2010). The epidemiology of traumatic brain injury. *Journal of Head Trauma and Rehabilitation, 25*(2), 72-80.

Crystal, S., Sambamoorthi, U., Walkup, J.T., & Akincigil, A. (2003). Diagnosis and Treatment of Depression in the Elderly Medicare Population: Predictors, Disparities, and Trends. *Journal of the American Geriatrics Society, 51*, 1718-1728.

Dawson-Hughes, B. & Josse, R. (2009). *Vitamin D status in North America.* International Osteoporosis Foundation. Retrieved from http://www.iofbonehealth.org/sites/default/files/PDFs/Vitamin_D_North_America.pdf

Dominick, C.H., Blyth, F.M., & Nocholas, M.K. (2012). Unpacking the burden: Understanding the relationships between chronic pain and comorbidity in the general population. *Pain, 153*, 293-304.

Feinstein, A. & Rapoport, M. (2000). Mild traumatic brain injury: The silent epidemic. Canadian *Journal of Public Health, 91*(5), 325-326.

Flaada, J.T., Leibson, C.L., Mandrekar, J.N., Diehl, N., Perkins, P.K., Brown, A.W. & Malec, J.F. (2007). Relative risk of mortality after traumatic brain injury: A population-based study of the role of age and injury severity. *Journal of Neurotrauma, 24*(3), 435-445.

Fletcher, P.C., Guthrie, D.M., Berg, K. & Hirdes, J.P. (2010). Risk factors for restriction of activity associated with fear of falling among seniors within the community. Journal of Patient Safety, 6(3), 187-191.

Fogelberg, D.J.., Hoffman, J.M., Dikmen, S., Temkin, N.R. & Bell, K.R. (2012). Associations of sleep and co-occuring psychological conditions at 1 year after traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 93*, 1313-1318.

Fried, L.P., Tangen, C.M., Waltson, J., Newman, A.B., Hirsch, C., ... McBurnie M.A.(2001). Frailty in older adults: evidence for a phenotype. *The Journals of Gerontology Series A: Medical Sciences, 56*(3), M146-M156.

Gatchel, R. & Turk , D.(1999*). Psychosocial factors in pain: critical perspectives.* New York: Guilford Press.

Gaubert-Dahan, M..L., Cougnaud-Petit, A., De Decker, L., Annweiler, C., Beauchet, O. & Berrut, G. (2011). Beyond to [sic] pattern of risk factors in elderly subjects. *Geriatrie et Psychologie Neuropsychiatrie du Vieillissement, 9*(3), 277-285.

Gould, K.R., Ponsford, J.L., Johnson, L. & Schonberger. M. (2011). Predictive and associated factors of psychiatric disorders after traumatic brain injury: A prospective study. *Journal of Neurotrauma, 27*(8), 1153-1163.

Gowing, R. & Jain, M.K. (2007). Injury patterns and outcomes associated with elderly trauma victims in Kingston, Ontario. *Canadian Journal of Surgery, 50*(6), 437-444.

Grimes, D.A. & Schulz, K.F. (2005). Compared to what? Finding controls for case control studies. *Lancet, 365*, 1429- 1433.

Guthrie, D.M., Fletcher, P.Cc, Berg, K., Williams, E., Boumans, N. & Hirdes, J.P. (2012). The role of medications in predicting activity restriction due to a fear of falling. *Journal of Health and Aging, 24*(2), 269-286.

Hardy, C. Kelly, K.D. & Voaklander, D. (2011). Does rural residence limit access to mental health services? *Rural and Remote Health, 11*(1766). Retrieved from http://www.rrh.org.au

Hart., T., Brenher, L., Clark, A.N., Bogner, J.A., Novack, T.A., Chervoneva, Nakase-Richardson, R & Arango-Lasprilla, J.C. (2011). Major and minor depression after traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 92,* 1211-1219.

Hickey, T., Speers, M.A. & Prohaska, T.R. (1997). *Public Health and Aging.* Baltimore MD: John Hopkins University Press.

Hoffman, J.M., Pagualayan, K.F., Zawaideh, N. Dikmen, S., Temkin, N & Bell, K.R. (2007). Understanding pain after traumatic brain injury: Impact on community participation. *American Journal of Physical Medicine and Rehabilitation*, 86(12), 962-969.

Jacob, H. (1984). *Using published data: errors and remedies.* London: Sage Publications.

Jacobs, J.M., Hammerman-Rozenberg, R. & Stessman, J. (2005). Longevity and chronic back pain in older people. *Journal of the American Geriatric Society, 53*(9), 1636-1637.

Jansson, C., Mittendorfer-Rutz, E & Alexanderson, K. (2012). Sickness absence because of musculoskeletal diagnoses and risk of all-cause and cause-specific mortality: A nationwide Swedish cohort study. *Pain, 153*, 998-1005.

Jordon, K.P. & Croft, P. (2010). Mortality and cancer in patients with new musculoskeletal episodes: A cohort study. *British Journal of General Practice, 60*(572), e105-e112.

Kannus, P., Niemi, Parkkari, J. Palvanen & Sievanen (2007). Alarming rise in fall-induced severe head injuries among elderly people. *International Journal of the Care of the Injured*, 38, 81-83.

Kannus, P., Parkkari, J., Siev., G., Heinon, A., Vuori, I. & Rvinen, M.J., (1996). Epidemiology of hip fractures. *Bone, 18*, 57s-63s.

Kraus, J. F, & MacArthur, D. L. (1996). Epidemiologic Aspects of Brain Injury. *Neurologic Clinics, 14*(2): 435-450.

Kroenke, K., Jianzhao, S., Oxman, T.E., Williams, J.W. & Dietrich, A.J. (2008). Impact of pain on the outcomes of depression treatment: Results from the RESPECT trial. *Pain, 134*, 209-215.

Lahz., S & Bryant, R.R. (1996). Incidence of chronic pain following traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 77*, 889-891.

Lancaster, B.P. (1999). *Defining and Interpreting Suppressor Effects: Advantages and Limitations.* Paper presented at the annual meeting of the Southwest Educational Research Association, San Antonio, Texas. ERIC Document Reproduction Service No. ED426097. Retrieved from: http://eric.ed.gov/PDFS/ED426097.pdf

Langlois, K., Greene-Finestone, L., Little, J., Hidiroglou N. & Whiting, S. (2010). *Vitamin D status of Canadians as measured in the 2007 to 2009 health measures survey.* (Statistics Canada Catalogue Number 82-003-X) Retrieved from http://www.statcan.gc.ca/pub/82-003-x/2010001/article/11131-eng.pdf.

Lee, E.T. (1980). *Statistical methods for survival data analysis.* Los Angeles, California: Lifetime Learning Publications.

Leblanc, J., De Guise, E., Goselin, N & Feyz, M. (2006). Comparison of functional outcome following acute care in young, middle-aged and elderly patients with traumatic brain injury. *Brain Injury, 20*(8), 779-790.

Leipzig. L.M., Cummings, R.G. & Tinetti, M.E. (1999). Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. *Journal of the American Geriatric Society, 47*(1), 30-39.

Leveille, S.G., Bean, J., Bandeen-Roche, K., Jone,s R., Hochber,g M. & Guralnik J.M.(2002) Musculoskeletal pain and risk for falls in older disabled women living in the community. *Journal of the American Geriatric Society, 50*(4), 671-678.

Leveille, S.G., Kiely, D.K., & Kiel, D.P. (2010). Chronic pain and the risk of falls in older adults [Letter to the editor]. *Journal of the American Medical Association, 303*(12), 1148-1149.

Leveille, S.G., Jones, R.N., Kiely, D.K. Hausdorff, J.M., Shmerling, R.H., Guralnik, J.M. .. Bean, J.F. (2009). Chronic Musculoskeletal Pain and the Occurrence of Falls in an Older Population. *Journal of the American Medical Association, 302*(20), 2214-2221.

Levin, H.S. McCauley, S.R., Pedroza Josic, C., Boake, C., Brown, S.A., Goodman, H.S., Brundage, S. (2005). Predicting depression following mild traumatic brain injury. *Archives of General Psychiatry, 62,* 523-527.

Masson, F., Thicoipe, M., Aye, P. , Mokni, T., Senjean, P. , Schmitt, V. ...Labadens, P. (2001). Epidemiology of severe brain injuries: A prospective population based study. *The Journal of Trauma Injury, Infection, and Critical Care, 51*(3), 481-489.

Maurice-Williams, R.S. (1999). Head injuries in the elderly. *British Journal of Neurosurgery, 13*(1), 5-8.

Menzel, C.J. (2008) Depression in the elderly after traumatic brain injury: A systematic review. *Brain Injury, 22*(5), 375-380.

Mernard, S. (1997). *Applied logistic regression.* Sage Publications: London.

Merskey, H., & Bogduk, N. (1994). Part III: Pain Terms, A Current List with Definitions and Notes on Usage. In H. Merskey & N. Bogduk (Eds.), Classification of chronic pain, IASP task force on taxonomy (2nd ed., pp. 209-214). Seattle, WA: IASP Press.

Mesrine, S., Boutron-Ruault, C.M., & Clavel-Hampton, F. (2010). Chronic pain and the risk of falls in older adults [Letter to the editor]. *Journal of the American Medical Association, 303*(12), 1147-1148.

Pagulayan K.F, Hoffman J.M., Temkin N.R., Machamer J.E. & Dikmen S.S. (2008). Functional limitations and depression after traumatic brain injury: Examination of the temporal relationship. *Archives of Physical Medicine and Rehabilitation, 89*(10), 1887-1892.

Palin, J.P., Koehoorn, M., Goldner, E.M., & Hertzmann, C. (2012) Prevalence and frequency of mental health care provided by general practitioners: differences between 2 national data sources for the same population. *Canadian Journal of Psychiatry, 57*(6), 366-74.

Pickett, W., Simpson, K. & Brison, R.J. (2004). Rates and external causes of blunt head trauma in Ontario: Analysis and review of Ontario trauma registry datasets. *Chronic Diseases in Canada, 25*(1), 32-41.

Pohar, M. Blas, M. & Turk, S. (2004). Comparison of logistic regression and linear discriminant analysis: A simulation study. *Advances in Methodology and Statistics, 1*(1), 143-161.

Preville, M. Boyer, R., Vasiliadis, H.M., Grenier, S., Streiner, D, Cairney, J. & Brassard, J. (2010). Persistence and remission of psychiatric disorders in the Quebec older adult population. *The Canadian Journal of Psychiatry, 55*(8), 514-522.

Pyo Hong, E. & Wan Park, J. (2012). Sample size and statistical power calculation in genetic association studies. *Genomics & Informatics, 10*(12), 117-122.

Ramage-Morin, P. (2008) *Chronic Pain in Canadian Seniors.* (Statistics Canada Catalogue Number 82-003-X) Retrieved from http://www.globalaging.org/health/world/2008/pain.pdf

Rapoport, M.J. (2012). Depression following traumatic brain injury. Epidemiology, risk factors, and management. *CNS Drugs, 26*(2), 111-121.

Rapoport, M.J. & Feinstein, A. (2000). Outcome following traumatic brain injury in the elderly: A Critical Review. *Brain Injury, 14*(8), 749-761.

Rapoport, M.J. & Feinstein, A. (2001). Age and functioning after mild traumatic brain injury: The acute picture. *Brain Injury, 15*(10), 857-864.

Rapoport, M.J., Herrmann, N., Shammi, P., Kiss, A., Phillips, A. & Feinstein, A. (2006). Outcome after traumatic brain injury sustained in older adulthood: A one-year longitudinal study. *American Journal of Geriatric Psychiatry, 14*(5), 456-465.

Rapoport, M.J, Kiss, A. & Feinstein, A. (2006). The impact of major depression on outcome following mild-to-moderate traumatic brain injury in older adults. *Journal of Affective Disorders, 92*, 273-276.

Rapoport, M.J., McCullagh, S., Shammi, P. & Feinstein, A. (2005). Cognitive impairment associated with major depression following mild and moderate traumatic brain injury. *The Journal of Neuropsychiatric and Clinical Neurosciences, 17*, 61-65.

Rapoport, M.J., McCullagh, S., Streiner, D. & Feinstein, A. (2003a).Age and major depression after mild traumatic brain injury. *American Journal of Geriatric Psychiatry, 11*(3), 365-369.

Rapoport, M.J., McCullagh, S., Streiner, D. & Feinstein, A. (2003b). The clinical significance of major depression following mild traumatic brain injury. *Psychosomatics, 44*(1), 31-37.

Ray, W.A., Purushottam, B.T. & Gideon, P. (2000). Benzodiazepines and the risk of falls in nursing home residents. *Journal of the American Geriatrics Society, 48*(6), 682-685.

Reitsma, M., Tranmer, J.E., Buchanan, D.M., & VanDenKerkhof, E.G. (2012). The epidemiology of chronic pain in Canadian men and women between 1994 and 2007: longitudinal results of the National Population Heath survey. *Pain Research and Management, 17*(3), 166-172.

Rodriguez & Ruigomez (2010). Case validation in research using large databases. *British Journal of General Practice*, 60(572), 160-161.

Rogers, J.M. & Read, C.A. (2007) Psychiatric comorbidity following traumatic brain injury. *Brain Injury, 21*, 1321-1333.

Rubenstein, L.Z. (2006). Falls in older people: Epidemiology, risk factors and strategies for prevention. *Age and Ageing, 34* (S2), ii37-ii41.

Rucker, D., Allan, J.A., Fick, G.H. & Hanley, D.A. (2002). Vitamin D insufficiency in a population of healthy western Canadians. *Journal of the Canadian Medical Association, 166*(12), 1517-1524.

Ruggeri, J. & Zou, Y. (2006). *Fiscal dimensions of population aging in canada*, University of New Brunswick, New Brunswick, Canada.

Sato, Y., Iwamoto, J., Kanoko, T. & Satoh, K. (2005). Low dose vitamin D prevents muscular atrophy and reduces falls and hip fractures in women after stroke: A randomized controlled trial. *Cerebrovascular Diseases, 20*(3), 187-192.

Satariano, W.A. (2006). *Epidemiology of aging: an ecological approach.* Jones and Bartlett Publishers, Toronto.

Selman & Benzel (1999). n*eurosurgical care of the elderly.* American Association of Neurosurgical Surgeons, Illinois, USA.

Shega, J.W., Dale, W., Andrew, M., Paice, J., Rockwood, K. & Weiner, D.K. (2012). Persistent pain and frailty: A case for homeostenosis. *Journal of the American Geriatric Society, 60*, 113-117.

Sibille, K. & McEwen, B. (2012). Authors build an important foundation for further research. *The Journal of Pain, 13*(12), 1269-1270.

Sjosten, N., Vaapio, S. & Kivel, S.L. (2008). The effects of fall prevention trials on depressive symptoms and fear of falling among the aged: A systematic review. *Aging & Mental Health, 12*(1), 30-46.

Skell, R.L, Johnstone B, Schopp L, Shaw J, & Petroski GF (2000). Neuropsychological predictors of distress following traumatic brain injury. *Brain Injury, 14*(8), 705-712.

Smith, B.H. (2012). This pain is killing me [commentary]. *British Journal of General Practice, 60*(572), e112.

Sosnoff J.J, Balantrapu, Ss, Pilutti, L.A., Sandroff, B.Mm, Morrison. S. & Motl, R.W. (in press). Cognitive processing speed is related to fall frequency in older adults with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation.* doi: 10.1016/j.apmr.2013.02.009

Stonnington, C.M. (2001). Depression and traumatic brain injury. *Brain Injury, 15*(7)561-562.

Stalenhoef., P.A., Diederiks, J.P., Knottnerus., J.A., Kester, A..D. & Crebolder, H.F. (2002). A risk model for the prediction of recurrent falls in community-dwelling elderly: A prospective cohort study. *Journal of Clinical Epidemiology, 55*(1), 1088-1094.

Strang, I., McMillan, R. & Jennet, B. (1978). Head injuries in accident and emergency departments at Scottish hospitals. *Injury, 10,* 154-159.

Streiner DL, Cairney J, Veldhuizen S. (2006). The epidemiology of psychological problems in the elderly. *Canadian Journal of Psychiatry, 51*(6), 404.

Stuck, A.E., Walhert, J.M., Nikolaus, T., Bula, C.J., Hohmann, C. & Beck, J.C. (1999). Risk factors for functional status decline in community living elderly people: A systematic literature review. *Social Science & Medicine, 48*, 445-469.

Sullivan, J.L., & Feldman, S. (1979). *Multiple indicators: an introduction.* London: Sage Publications.

Sutton, Moldofsky, H. & Badley, E.M. (2001). Insomnia and health problems in Canadians. *Sleep, 24*(6), 665-670.

Szczerbińska, K., Hirdes, J.P. & Zyczkowska, J.(2012) Good news and bad news: depressive symptoms decline and undertreatment increases with age in home care and institutional settings. *American Journal of Geriatric Psychiatry, 20*(12), 1045-1056.

Tabachnick, B.G. & Fidell, L.A. (2001). *Multivariate statistics.* London: Pearson.

Tai-Seale, Bolin, Bao & Street (2011). Management of chronic pain among older patients: Inside primary care in the US. *European Journal of Pain, 15*, 1087.e1-1087.e8.

Tannenbaum, C., Lexchin, J., Tamblyn, R. & Romans, S. (2009). Indicators for measuring mental health: Towards better surveillance. *Health Care Policy, 5*(2), e177-e186.

Thapa, P., Gideon, P., Cost, T.W., Milam, A., Pharm, D., & Ray, W.A. (1998). Antidepressants and the risk of falls among nursing home residents. *New England Journal of Medicine, 339*(13), 875-882.

Thompson, H.J., McCormick, W.C., Kagan, S.H. (2006). Traumatic brain injury in older adults: Epidemiology, outcomes and future implications. *Journal of the American Geriatric Society. 54*(10), 1590-1595.

Topinkova, E. (2008). Aging, disability and frailty. *Annals of Nutrition & Metabolism, 52*(1), 6-11.

Torrance, N., Elliott, A.M., Lee, A.J., & Smith, B.H. (2010). Severe chronic pain is associated with increased 10 year mortality. A cohort record linkage study. *European Journal of Pain, 14*, 380-386.

Turner, J.A. (In press) Research on cognitive-behavioral therapies for older adults with chronic pain: In its infancy, but growing. *Pain.* Retrieved from doi: http://dx.doi.org/10.1016/j.pain.2013.02.028

van den Berg, M. et al (2011). Depression after low-energy fracture in older women predicts future falls: a prospective observational study. *BMC Geriatrics, 11*(73). Retrieved from http://www.biomedcentral.com/1471-2318/11/73

van der Wint, D. (2012). The role of co-morbidity in accumulating risk of chronic pain. *Pain, 153,* 259-260.

Vassallo, J.L., Proctor-Weber, Z., Lebowitz, B.K., Curtiss, G. & Vanderploeg, R.D. (2007). Psychiatric risk factors for traumatic brain injury. *Brain Injury, 21*(6), 567-573.

Vieth, R., Cole, D.E., Hawker, G.A., Trang., H.M. & Rubin, L.A. (2001). Wintertime vitamin D insufficiency is common in young Canadian women, and their vitamin D intake does not prevent it. *European Journal of Clinical Nutrition, 55*(12), 1091-1097.

Vink, D., Aartsen, M.J., & Schoevers, R.A. (2008). Risk factors for anxiety and depression in the elderly: A review. *Journal of Affective Disorders, 106*(1-2), 29-44.

Voaklander D.C., Kelly K.D., Rowe B.H., Schopflocher D.P., Svenson L., Yiannakoulias N, & Pickett W. (2002). Pain, medication, and injury in older farmers. *American Journal of Industrial Medicine, 49*(5), 374-82.

Wade, D.T., King, N.S., Wenden, F.J., Crawford, S. & Caldwell, F.E. (1998). Routine follow up after head injury: A second randomized controlled trial. *Journal of Neurology, Neurosurgery & Psychiatry, 65,* 177-183.

Wallace, R.B. & Woolson, R.F. (1992). *The epidemiologic study of the elderly.* New York, New York: Oxford University Press.

Whelan-Goodinson, R., Ponsford, J. & Schonberger, M. (2008). The association between psychiatric state and outcome following traumatic brain injury. *Journal of Rehabilitation Medicine, 40*(10), 850-857.

Wilber, S.T., Sullivan, A.F., & Camargo, C.A. (2010). Chronic pain and the risk of falls in older adults [Letter to the editor]. *Journal of the American Medical Association, 303*(12), 1148.

Wilson, JA, Pentland, B., Curet C.T., & Miller, J.D. (1987). The functional effects of head injury in the elderly. *Brain Injury, 1*, 183-188.

Wolfson, M.C. (1996). Health-adjusted life expectancy. *Health Reports, 8*(1). Retrieved from http://www.statcan.gc.ca/pub/82-003-x/1996001/article/2825-eng.pdf

Wong, P.P., Dornan, J., Schentag, C.T., Ip, R. & Keating, A.M. (1993). Statistical profile of traumatic brain injury: A Canadian rehabilitation population. *Brain Injury, 7*(4), 283-294.

Ziere, G., Deileman, J.P., Hofman, A., Pols, H.A.P., van der Cammen, T.J.M. & Stricker, B.H.CH. (2005). Polypharmacy and falls in the middle age and elderly population. *British Journal of Clinical Pharmacology, 61*(2), 218-223.

Appendix A Anxiety Pharmacare Criteria

Bromazepam = 518123, 2177161, 518131, 682314, 2167808, 2167816, 2167824, 2171856, 2171864, 2171872, 2177153, 2177188, 2192705, 2192713, 2192721, 2330584, 2330585

Alprazolam = 548359, 677485, 865397, 1913484, 865400, 813958, 548367, 677477, 723770, 1913239, 1913247, 1913492, 02137534, 02137542

Chlordiazepoxide = 20923, 522988, 522988, 12629, 20931, 12637, 12645, 13218, 13463, 13471, 13498, 20915, 20915, 20923, 20931, 134341, 156590, 235873, 251267, 267090, 295051, 363596, 398411, 430927, 430935, 451479, 522724, 522996

Clonazepam = 2179660, 382825, 2048701, 2103656, 2177889, 2207818, 2230950, 382841, 2048736, 2048728, 3103737, 2173344, 2173352, 2230366, 2230368, 2230369, 2230950, 2230951

Diazepam = 272450, 405337, 405329, 272434, 272442, 362158, 399728, 13277, 13285, 13293, 13757, 13765, 13773, 272639, 272647, 276642, 276650, 280429, 299545, 303461, 311596, 313580, 315052, 315079, 396230, 432377, 432385, 432393, 434388, 434396, 466891, 466905, 891797

Lorazepam = 399124, 655740, 711101, 722138, 865672, 2041456, 348325, 637742, 655759, 865680, 2041464, 557757, 348333, 637750, 655767, 2041421, 2041472, 577765, 655651, 728187, 728195, 728209, 865699, 2041413, 2041448

Oxazepam = 402680, 500852, 295698, 402745, 496529, 402737, 496537, 231363, 295701, 414247, 414255, 414263, 483893, 483907, 483915, 497762, 497770, 568392, 568406, 568414, 726370, 2043653, 2043661, 2043668

Clorazepate = 264911, 264938, 264946, 628190, 628204, 628212, 860689, 860697, 860700

Rule 1: Any 2 prescriptions within a 30 day period. Ok if same group, but must be different number (e.g. not a repeat of the exact same).

Appendix B Insomnia Pharmacare Criteria

Group 1: (Dinpin) = 20893, 792659, 811882, 443158, 512559, 614378, 808563, 808571, 872423, 872431, 511528, 511536, 604453, 604461, 2225964, 2225972, 2229455, 2229456, 1926799, 2008203, 2218313, 2238596, 12696, 12718, 496545, 496553, 521698, 521701, 86, 581291, 581305, 15261, 15288, 21032, 37400, 335053, 37419, 335061, 37427, 335088, 354295, 754129, 579378, 1937235, 2144271, 2147645, 702277, 2147653, 579351, 1937227, 2144263, 2147637, 2231683, 1913433, 2049996, 1913425, 2050013, 1913441, 00128864, 02050005

Group 2: (dinpin)= 518123, 2177161, 548359, 677485, 865397, 1913484, 865400, 813958, 20923, 522988, 522988, 12629, 20931, 2179660, 382825, 2048701, 2103656, 2177889, 2207818, 2230950, 382841, 2048736, 272450, 405337, 405329, 272434, 272442, 362158, 399728, 13277, 13285, 13293, 399124, 655740, 711101, 722138, 865672, 2041456, 348325, 637742, 655759, 865680, 2041464, 557757, 348333, 637750, 655767, 2041421, 2041472, 402680, 500852, 295698, 402745, 496529, 402737, 496537, 231363

Rule 1: Any of Group 1 meets the criteria for insomnia.

Rule 2: Any of Group 2 meets the criteria for insomnia

IF quantity dispensed is equal or greater to 90.

Any tranquilizer prescribed for a one a day dosage is most likely to be used for sleep. Low dose sedating antidepressants (Under a therapeutic dose) may be prescribed for sleep, chronic pain, or both.

Prescriptions considered markers of insomnia include sleeping pills such as Chloral Hydrate (500mg), Temazepam (aka Restoril, hypnotic, 15-30mg), Triazolam (Aka Starnoc, .125-.25mg), Zopiclone (aka Immovane, Tranquilizer, 7.5mg), Flurazepam (Aka Dalmane, hypnotic, 30mg), Secobarbital (Aka Seconal, Hypnotic, 100mg), Amibarbital/seconal combination (aka Tuinal, 100mg) and Pentobarbital (Aka Nembutal, short term hypnotic, 100mg).

Appendix C Depression Pharmacare Criteria

Set 1 dinpin: 16349, 37427, 271152, 335088, 377899, 456349, 654507, 354295, 405612, 754129, 10480, 21520 , 209848, 236721, 326852, 377929 , 456357, 306487, 405604, 644579, 726303, 306495, 353876, 893765, 1946277, 1948792, 2024918, 2099136, 2211955, 2216264, 2223333, 425265, 1946242, 1948806, 2024926, 2099144, 2211963, 2216272, 2223368, 878782, 1948814, 2103591, 2211971, 2216280, 2013605, 24341, 629286, 842761,1913433, 2050013, 2140101, 2144158, 400750, 629294, 842788, 1913441, 2050021, 2140128, 326925, 629308, 842796, 1913468, 2050048, 584274 , 1913476, 2050056, 25844, 740810, 762621, 1926330, 1940449, 2020610, 442437, 761656, 1926349, 2070987, 25852, 740829, 761648, 1926284, 1940457,2020629, 402591, 2040751, 2139367, 2230065, 2229590, 2230065, 2229590, 2147653, 579378, 1937235, 2053195, 2144271, 2147645, 2165392, 2230285, 702277, 2053209, 2144298, 2147653, 2165406, 2230286, 824135, 641855, 2158604, 360481, 360481, 2158612, 360503, 2158620, 360511, 2158639, 27111, 1919598, 264148, 476552, 899348, 899356 2166747, 2218410, 2232148, 2232150, 636622 1917021 2018985, 2155826, 2155834 2177579, 2177587, 2192764, 2216353, 2216361, 2216582, 2216590, 2237813, 2237814, 2245281, 1911856, 1919342, 2218453, 2231329, 2240850, 2240724, 2257688, 1911872 1919369, 2218461, 2231330, 1940481, 1940473, 00024406, 00236683, 00328782, 00328790, 00406775, 00461733, 00590665, 02011239, 02013231, 02074834, 02216132, 02216140, 02216159, 322741, 32226, 527084, 2169886, 527092, 2169894, 527106, 2169908, 527114, 27111, 1919598, 264148, 476552, 899348 899356 2166747,2218410 2232148 2232150, 2302535, 2302543, 2239607, 2245202, 2087294, 2087375, 2237398, 2242823, 2245102, 2245203, 2245435, 2245755, 2246549, 2087383, 2237399, 2242824, 2245103, 2245204, 2245436, 2245756, 2246550, 2087391, 2237400, 2242825, 2245111, 2245205, 2245437, 2245757, 2246551, 1962817,

2238281, 2240484, 1962779, 2238282, 2240481, 1962787, 1962795, 2103702, 2237280, 2237282, 2237825, 2296683

Set 2 dinpin: 16330, 37419,251275, 306320, 335061, 371009, 377880, 446459, 448818, 1985426, 654515, 1985426, 10472, 21512, 209864, 235776, 236756, 312797, 371025, 377910,431087, 10448, 353868, 1946269, 1948784, 2024896, 2099128, 2211947,2216256, 2223325, 15237, 2177706, 2223147, 2223538, 2230362, 24333, 629278, 842753, 1913425, 2050005, 2140098, 2144131, 25836, 740802,761613, 1926322, 1940430, 2020602, 279277, 324019, 2040778, 2130165, 2139359, 579351, 1937227, 2053187, 2144263, 2147637, 2165384, 2231683, 2230284, 2027887, 1962779, 2132702, 2238280, 2240485, 2103680, 2103699

Set dinpin: 16322, 18325, 37400, 293911, 335053, 370991, 448796, 654523, 16306, 10464, 21504, 209856, 236748, 360201, 377902, 776157, 1946250, 1948776, 2024888, 2103583, 2211939, 2216248, 2223341, 15229, 2177692,2223139, 2223511, 2230361, 2231686, 24325, 629251, 842745, 2049996, 2140071, 2144123, 330566,2040786, 2139340, 2230064, 25828, 740799, 761605, 761702, 1926357, 2020599

Rules:

Rule 1: If any in set 1, this is a case of depression.

Rule 2: if any in set 2 AND quantdis is => 60, this is a case of depression.

Rule 3: if any in set AND quantdis =>120, this is a case of depression.

Ascertaining depression cases through the Pharm database was a time-consuming process. Many depression medications can have alternate uses, especially at low doses (e.g. anxiety, sleep, etc). The type of medication, and also the amount (strength and pills per day) had

to be taken into account in forming not only the depression criteria, but the anxiety and insomnia criteria as well. Therefore each medication was examined and decided on an individual basis, with the help of a medical professional. Criteria used and reasoning discussed were as follows:

Tricyclic Antidepressants

In low doses Tricyclic Antidepressants (TCA's) are ineffective as antidepressants, and more often used in the treatment of insomnia, fibromyalgia or diabetic neuropathy. A dosage of 50mg or more a day (based on number/strength per day of prescription period) is larger than is commonly used for insomnia, and was taken as in indication of depression. Examples would include Amitriptyline, Imipramine, Clomipramine, Trimipramine and Desipramine. The TCA Noratryptyline has no sedative properties. As it is also a preferred drug in treating depression in the elderly, use of noratryptyline itself was considered a marker of depression.

Selective Serotonin Uptake Inhibitors (SSRI's)

SSRI's are largely used for depression even when used at lower doses. For example Prozac (Fluoxetine) is not used for sedative purposes. A prescription of SSRIs was considered a marker of depression. 50mg or more of Sertraline, Doxepine, or Noritryptyline was considered more than likely to be an antidepressant dose. A prescription of a daily dose of 20mg or more of Paroxetine was considered a therapeutic dose.

MAO Inhibitors

MAO Inhibitors such as Nardil, and Moclobemide (a selective MAO) are used only in depression and therefore used as markers of depression.

Other Antidepressants

Any prescription of Lithium Carbonate was used as a marker for Bipolar Disorder. A prescription of 50mg or more per day of Doxepine was considered a dosage large enough to be

of therapeutic use in depression rather than insomnia. A prescription of 100mg or more/day of Trazadone was used as a marker for depression. This cut-off is higher than the doses of other antidepressant groups as, in the elderly, doses under 100mg may be used as a treatment for insomnia. Both Fluvoxamine and Ludiomel are only recommended for depression and therefore were used as markers of depressionas were Protriptyline and Amoxapien. The same is true of Wellbutrin. The SNRI Effexor was considered to be clearly for antidepressant use at doses of 75mg and up. Mirtazapine Remeron was considered to be used as an antidepressant at any dose (30mg was the only dose) at the time. While it is currently used as an anti-anxiety medication, at the time it was used only as an antidepressant.

Appendix D Chronic Pain Pharmacare Criteria

The goal is to identify chronic pain cases in pharmacy data by first identifying prolonged pain, and then pulling those who identified as having severe pain out of that group (hence the two terms, chronic and pain).

What is wanted are chronic pain cases that either started before day 0 (day of head injury) or after, not those met the chronic criteria crossing day 0. You may have to run this once for before day 0 and once for after day 0.

There are two criteria they must meet: at least one each of the prolonged criteria, followed by any of the severity criteria.

****

T3 = 176192, 261432, 261459, 372358, 396516, 425389, 608181, 608203, 608882, 653276, 666130, 687219, 706523, 1934791, 2163926

T2 = 00003220, 00018686, 00023647, 00093122, 00396680, 00593435, 00604623, 00779458, 00095508, 00108103, 00132594, 00293504, 00372331, 00425370, 00440809
00604496, 00653241, 00687200, 00693952, 00706515, 02163934, 00176192, 0060820, 00108316, 00172421, 01934783

K = 864048, 2162660

OP = 00010014, 00003506, 00033685, 00041513, 01928392, 02138018, 00125083, 00125121, 00290572, 00290602, 00622133, 00627100, 00705438, 00786543, 00885401, 00885428, 00885436, 00885444, 01916270, 01916289 , 02125323, 02125331, 02125358, 02125366, 02125374 , 02125382, 02125390, 00033731, 01904965, 02137984, 00229210
00594636, 00594644, 00594652, 00624268, 00626384, 00626392, 00665134, 00665142

00665150, 00675962, 00690198, 00690201, 00690228, 00690244, 00776181, 00776203
01909371, 01909398, 01909401, 01909428, 01916262, 01916319, 01988727, 01988735
01988743, 02009706, 02009749, 02009765, 02009773, 02014203, 02014211, 02014238
02014254, 02014297, 02014300, 02014319, 02014327, 02015439, 02019930, 02019949
02177749, 00443948, 00789739, 00103535, 00103543, 00389641, 00389668, 00574384
00574392, 00580201, 00580228, 00580236, 00580244, 00608157, 00608165, 01916327,
01916475, 01916483, 01916491, 01916548, 01916556, 01916572, 1937383, 01937391
01937413, 00197405

Note: Opioids does not include: Opioid cough syrup, injections, or suppositories.

NSAID = 00252409, 00327794, 00364142, 00441643, 00441651, 00443182, 00443190,
00443204, 00484911, 00506052, 00585114, 00606197, 00606200, 00606219,
00606227, 00629324, 00629332, 00629340, 00629359, 00636517, 00636533, 00658804
00793183, 00842877, 00846325, 00846481, 00851701, 01933531, 01933558, 01994352
02020696, 02020718, 02150794, 02186934, 02187124, 00514004, 00514012, 00590827
00632724, 00632732, 00782459, 00808539, 00808547, 00839175, 00839183, 00870951
00870978, 00886017, 00886025, 02048698, 02091194, 02158582, 02162814, 02174677
02174685, 01917056, 02229837, 00432369, 00456888, 00745588, 00745596, 00778354
00778362, 00808636, 02042576, 02042584, 00525596, 00525618, 00632708, 00632716
00642886, 00642894, 00695696, 00695718, 00836230, 00836249, 00865761, 00865788
02139952, 02139960, 02144212, 02144220, 02154420, 02154463, 02171813, 02171821
00593346, 00593354, 00600792, 00647942, 00675199, 00675202, 01912038, 01912046,
02020661, 02020688, 02100509, 02100517, 02223066, 02223074, 00516783, 00638668
00754153, 01902717, 01902725, 02017628, 02017636, 00016039, 00016047, 00016233

00337420, 00337439, 00463248, 00594458, 00594466, 00611158, 00611166, 00646261

00865850, 00865869, 01934139, 01934147, 02143364, 02143372, 02146932, 02146940

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01913050, 01913069, 01913077, 01926365, 01926373, 01926381, 01926403, 01926411

01931512, 01981528, 01981536, 02015951, 02031175, 02044633, 02044641, 02044781

02084171, 02084198, 02150808, 02150816, 02150824, 02156083, 02165481, 02172577

02183099, 02183102, 00588989, 00884367, 00328642, 00345504, 00299413, 00335193

00491772, 00522651, 00522678, 00525537, 00531022, 00565350, 00565369, 00583367

00587923, 00589861, 00590754, 00590762, 00592277, 00600806, 00615307, 00615315

00615323, 00615331, 00618721, 00627097, 00655686, 00675369, 00756814, 00778389,

00784354, 00788767, 00865621, 00865648, 00865656, 00865664, 00869031, 00887056,

01900897, 01937332, 01937340, 01937359, 01940309, 02017237, 02026600, 02162415

02162423, 02162431, 02162458, 02162466, 02162474, 02162482, 02162490, 02162717,

02162725, 02162792, 02168871, 00155225, 02229452, 02229569, 02083531, 02083558,

00589926, 00589934, 00893714, 01924613, 01924621, 01989774, 01989782, 01989790

02136112, 02136120, 02179679, 02179687, 02221942, 02221950, 02221969

Prolonged criteria:

Rule 1: Have it start over counting at day 0 (See days column 53) so the pain criteria are either met completely before day 0 or after day 0.

Rule 2: Any of Group 1 meet the prolonged criteria:

IF: Three or more billings in dinpin for any groups (may be from a mix of categories)

AND IF: The dinpins are separated by at least 3 weeks over a 3 month period, followed by another of the same code within a year of the initial coding.

Rule 3: Any of Group 2 meet the prolonged criteria

IF: four or more billings within one year

AND IF: each dinpin is separated by at least 6 weeks.

Prolonged Pain Criteria from ICD-9 codes:

ICD-9 billings for musculoskeletal disorders in the hospital or medical billings files provided they fell in the same pattern as either rule 2, or rule 3 above. ICD-9 codes used: 710-739 (inclusive), 784, 346.

END PROLONGED CRITERIA

Once they have met ANY OF THE ABOVE the prolonged criteria, please run that group through the severity criteria. Those that meet BOTH sets are chronic pain cases.

Severity criteria

Rule 1: Have it start over counting at day 0 so the pain criteria are either met completely before day 0 or after day 0.

Rule 2: Any OP

Rule 3: OR (THREE OR MORE T3)

Rule 4: OR (ONLY TWO T3 AND ONE OR MORE T2; See dinpin list above)

Rule 5: OR (ONLY TWO T3 AND ONE or MORE K; see dinpin list above)

Rule 6: OR (ONLY TWO T3 AND ANY NSAID; see dinpin list above)

Rule 7: OR (ONLY ONE T3 AND THREE OR MORE NSAID; see din list above).

Rule 8: OR (NSAID >= 4 TIMES; see dinpin list above)

Rule 9: OR (T3 >= 50 in column quantity dispensed (see dinpin list above)